

Ole Christian Mjølstad

# Pocket-size ultrasound, a new diagnostic tool in clinical practice

Thesis for the degree of Philosophiae Doctor

Trondheim, December 2013

Norwegian University of Science and Technology  
Faculty of Medicine  
Department of Circulation and Medical Imaging

St. Olavs Hospital / Trondheim University Hospital  
Department of Cardiology



**NTNU – Trondheim**  
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**ST. OLAVS HOSPITAL**  
TRONDHEIM UNIVERSITY HOSPITAL

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## **Norsk sammenfatning:**

### **Lommeultral lyd, et nytt diagnostisk verktøy i klinisk praksis.**

Ultralyd og ekkokardiografi har vært viktige verktøy i vår kliniske hverdag i flere tiår. Det har i all hovedsak vært utført av høyt spesialisert personell i spesialiserte laboratorier. I løpet av de siste 20 år har det vært en formidabel teknologisk utvikling – dette har gjort det mulig å produsere ultralydapparat på størrelse med en mobiltelefon (lommeultral lyd). Dette er maskiner med redusert funksjonalitet sammenliknet med en standard ultralydmaskin. Blant de som er tilgjengelig på markedet per i dag har alle «levende» todimensjonal avbildning og en leverandør har utstyr med «levende» fargeavbildning av blodstrøm (farge Doppler). De er svært portable har et enkelt brukergrensesnitt og har en relativt lav pris (ca. 50 000 NOK) sammenliknet med en standard ultralydmaskin – de er således tilgjengelige for mange flere brukere både i og utenfor sykehus.

Flere studier har vist god bildekvalitet og god evne til å vurdere anatomi og funksjon av hjertet, brysthule og bukorgan i samsvar med standard ultralyd. Begrensingene sammenliknet med standard ultralydmaskiner er først og fremst i forhold til manglende tilleggsfunksjoner, deriblant mulighet for måling av blodstrømhastighet (spektral Doppler). Dette medfører at f.eks. klaffefunksjon må kvantiteres basert på skjønn ut ifra bildeinformasjon og ikke målinger.

I dette arbeidet på 4 delstudier har vi studert om ikke-eksperter og eksperter kan nyttiggjøre seg lommeultral lyd i ulike kliniske situasjoner. Kvaliteten av undersøkelsene og om undersøkelsene kan medføre bedret diagnostikk har vært hovedfokus.

### **Artikkel 1:**

Vi ønsket å se hvordan allmennleger uten erfaring med ultralyd var i stand til å vurdere venstre ventrikkels systoliske funksjon hos pasienter med kjent eller med risiko for å utvikle hjertesvikt. Etter en kort, men svært målrettet opplæring, ble 92 pasienter inkludert. I 87 % av pasientene var allmennlegen i stand til å registrere og bedømme venstre hjertekammers funksjon ut ifra systolisk forkortning i lengdeaksen (mitral annulus ekskursjon (MAE) i apikalt 4-kammerbilde). Man fant ingen signifikante forskjeller mellom MAE målt av allmennleger og målt av kardiolog. Det var heller ingen signifikante forskjeller i MAE om opptaket var utført av allmennlege ved bruk av lommeultralyd eller kardiolog ved bruk av en standard ekkomaskin.

### **Artikkel 2:**

Subjektiv vurdering er en utfordring innen ekkokardiografi og sannsynligvis av enda større betydning når bruker er uerfaren. Vi testet ut en automatisk algoritme som følger klaffeplanet mellom venstre forkammer og hjertekammer og således gir et mål for venstre hjertekammers systoliske forkortning (MAE). Vi fant god overensstemmelse sammenliknet med referansemetode som var MAE målt av kardiolog ved bruk av «motion-mode». Det var best samsvar når man anvendte kun isolert septal registrering.

### **Artikkel 3:**

Pasienter innlagt ved medisinsk avdeling ved Sykehuset Levanger, Helse Nord-Trøndelag HF, ble undersøkt med lommeultralyd (hjerte, pleura og store kar i abdomen) etter at de var undersøkt og vurdert etter gjeldende retningslinjer. Undersøkelsen ble utført av leger i spesialisering etter en målrettet opplæring i diagnostisk bruk av ultralyd, inkludert en supervisert treningsperiode. Venstre hjertekammer, hjerteposen og lungesekken ble riktig

bedømt i samsvar med referanse hos > 95 % av pasientene. Bedømmelse av sykdom i aortaklaffen viste godt samsvar, bedømmelse av klaffe lekkasjer mellom hjertekamre og forkamre, samt venstre forkammers størrelse viste moderat samsvar. Ingen alvorlig sykdom ble oversett.

#### **Artikkel 4:**

Pasienter innlagt ved medisinsk avdeling ved Sykehuset Levanger, Helse Nord-Trøndelag HF, ble undersøkt med lommeultral lyd med tanke på sykdom i hjerte, brysthule (pleura) og buk inkludert de store blodkar. Undersøkelsene ble utført av kardiologer erfarne i bruk av ultralyd etter at de var undersøkt og vurdert av vakthavende leger etter gjeldende retningslinjer. 196 pasienter ble undersøkt og resultatene av lommeultral lydundersøkelsen samsvarte godt med referanseundersøkelse. I 18 % av pasientene ble diagnosen endret, hos 19 % ble diagnosen bekreftet og hos 9 % ble en relevant tilleggsdiagnose påvist. Undersøkelsen tok < 10 minutter.

**Navn kandidat:** Ole Christian Mjølstad

**Institutt:** MI lab, Institutt for sirkulasjon og bildediagnostikk, DMF, NTNU

**Hovedveileder:** Post. Doc Bjørn Olav Haugen, Institutt for sirkulasjon og bildediagnostikk, DMF, NTNU.

**Biveiledere:** Professor Hans Torp, Institutt for sirkulasjon og bildediagnostikk, DMF, NTNU, professor Olav Haraldseth, Institutt for sirkulasjon og bildediagnostikk, DMF, NTNU og professor Anders Grimsmo, Institutt for samfunnsmedisin, DMF, NTNU

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## List of papers

1: Mjølstad OC, Snare SR, Folkvord L, Helland F, Grimsmo A, Torp H, Haraldseth O, Haugen BO. Assessment of left ventricular function by GPs using pocket-sized ultrasound. *Fam Pract.* 2012;29:534-40.

2: Snare SR, Mjølstad OC, Orderud F, Haugen BO, Torp H. Fast automatic measurement of mitral annulus excursion using a pocket-sized ultrasound system. *Ultrasound Med Biol.* 2011;37:617-31.

3: Mjølstad OC, Andersen GN, Dalen H, Graven T, Skjetne K, Kleinau JO, Haugen BO. Feasibility and reliability of point-of-care pocket-size echocardiography performed by medical residents. *Eur Heart J Cardiovasc Imaging.* 2013;14:1195-1202.

4: Mjølstad OC, Dalen H, Graven T, Kleinau JO, Salvesen Ø, Haugen BO. Routinely adding ultrasound examinations by pocket-sized ultrasound devices improves in-patient diagnostics in a medical department. *Eur J Intern Med.* 2012;23:185-91.

## Selected abbreviations

2 D	Two dimensional	ICU	Intensive care unit
AA	Abdominal aorta	IVC	Inferior Vena Cava
ASE	American Society of Echocardiography	LA	Left Atrium
CF	Colour Doppler	LV	Left ventricle (ventricular)
CI	Confidence interval	LVEF	Left ventricular ejection fraction
EACVI	European Association of Cardiovascular Imaging	MAE	Mitral annular excursion
EAE	European Association of Echocardiography.	Pocket- size	Pocket-size ultrasound
FAST	Focused Assessment with Sonography in Trauma	OR	Odds Ratio
GP	General practitioner	RV	Right ventricle (ventricular)
HF	Heart Failure	SD	Standard deviation

# **1 Introduction**

## **1.1 Selected history of ultrasound.**

Ultrasound is defined as sound with a frequency above that which humans can hear, or more than 20,000 Hz (20 kHz). Ultrasonography was established more than half a century ago. Since then, this non-invasive imaging modality has been widely used in many clinical disciplines (radiology, cardiology, emergency medicine and gynaecology/obstetrics among others). Its development has closely paralleled the advances in electronics and computer technology and is an example of the interaction and co-operative efforts of engineers, physicists and clinicians. In 1953, Edler first described cardiac structures by the ultrasound reflectoscope (1). Real-time 2-dimensional (2D) images were presented by Hertz and Aasberg in 1967. Since then, the development of ultrasound has been tremendous and worldwide. Liv Hatle and Bjørn Angelsen made important contributions in establishing Doppler as a tool for diagnosing and monitoring cardiovascular disease (2-5). Clinical studies have been published since the mid-70s showing how echocardiography should be the method of choice, gradually replacing cardiac catheterisation in a number of non-coronary cardiovascular diseases. The most recent years have seen advances in functionality like 3-dimensional ultrasound, the use of ultrasound contrast and deformation imaging.

## **1.2 Pocket-size ultrasound devices**

Within the last two decades, the size of a standard laboratory echo machine has been considerably reduced from the size of a household refrigerator to the size of a laptop computer. The down-sizing of scanners has branched in 2 directions: 1) the laptop echo machines, which are smaller and less expensive systems, still featuring most of the advanced technology with at least pulsed and continuous wave Doppler, M-mode and often tissue Doppler mode; and 2) true pocket-size scanners (Figure 1).

Figure 1: Illustration of the use of pocket-size ultrasound



**Figure 1:** Demonstration of the pocket-size device Vscan. Illustration from MI Lab, Norwegian University of Science and Technology (Photo: Geir Mogen).

With the development of 3-dimensional ultrasound, electronic components had to be removed from the scanner and placed in the ultrasound probe. This, in combination with the growth of cellular phone technology, has made the extreme miniaturisation process possible. These devices have a very limited range of functionality compared to the above-mentioned standard laboratory echo machine (Table 1).

Table 1. Functionality of high-end versus pocket-size scanners.

<p style="text-align: center;"><b>High-end scanner</b></p> <p style="text-align: center;"><b>Vivid 7 (GE Healthcare)</b></p>	<p style="text-align: center;"><b>Pocket-size scanner</b></p> <p style="text-align: center;"><b>Vscan (GE Healthcare)</b></p>
<ul style="list-style-type: none"> <li>• H x W x D: 1.58 x 0.64 x 0.89m</li> <li>• Weight: 191 kg</li> <li>• M-Mode, B-mode – 2D imaging, Harmonic imaging, Colour flow, Power Doppler, Pulsed Doppler, Continuous Doppler, Tissue Doppler, Tissue type imaging, Strain rate imaging, Tissue synchronisation imaging.</li> <li>• Digital Beam former with 1024 channels technology.</li> <li>• Probes: Multi-frequency, linear, convex, phased array, sector.</li> </ul>	<ul style="list-style-type: none"> <li>• H x W x D: 135 x 73 x 28 mm</li> <li>• Weight: 390 g</li> <li>• B-mode – 2D imaging, Harmonic imaging, Colour flow.</li> <li>• 64 elements</li> <li>• Phased array probe, fc 2.5 MHz</li> <li>• Frame rate 20 Hz</li> <li>• Sector 75 degrees.</li> <li>• Scan depth max 25 cm</li> </ul>

**Table 1:** Differences between a high end scanner (Vivid 7, GE Healthcare, Horten, Norway) and a pocket-size scanner (Vscan, GE Healthcare, Horten, Norway). H: height; W: width; D: depth.

Pocket-size ultrasound devices fit in a white coat pocket, they are usually priced below \$10,000 and they can be operated easier than a standard smart-phone. There are several such devices on the market. In 2007, Siemens released their Acuson P10 and in October 2009, Jeff Immelt, as the CEO of General Electric, presented the Vscan (GE Healthcare, Horten, Norway). One of the latest releases is the MobiUS SP1 from MobiSante which is a smart-phone-based system which simply involves connecting the probe. Figure 2 shows some of the available scanners (6).

Figure 2. Different pocket-size devices.



**Figure 2:** Commercially available pocket-size devices from four different vendors. (A) Vscan™ (GE Healthcare, Horten, Norway). (B) MobiUS™ (SP1, MobiSante, Inc., Redmond, WA, USA). (C) Acuson P10™ (Siemens Medical Solutions Inc. Malvern, PA, USA). (D)

Signos™ (Signostics Ltd, Thebarton, Australia). The impression of the relative sizes of the devices may be incorrect. Reproduced from (6) with permission from Expert Reviews Ltd.

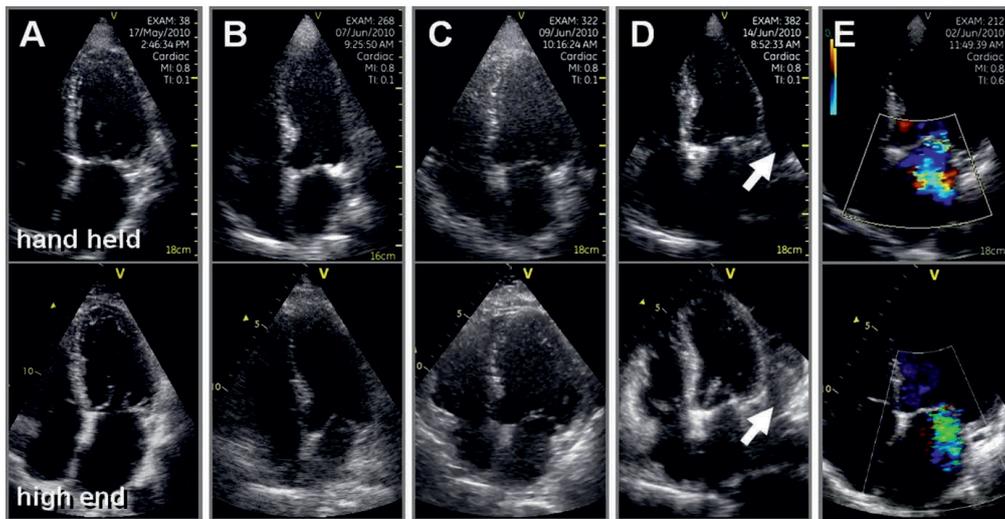
All of these devices offer 2D imaging and the Vscan also has the capacity for simplified colour Doppler (CF) (Table 2). The image quality of pocket-size scanners has been shown in several studies to be excellent, and only in patients with very bad echogenicity have the high-end scanners shown better image quality (7) (Figure 3). These devices may therefore be used by the physician almost everywhere and are well suited as an efficient tool during busy ward rounds in different clinical departments.

Table 2. Technical data of different pocket-size echocardiographic devices.

	Imaging modes	Transducer (MHz)	Display	Total weight	Patient identification	Storage	Batt. capacity (scan time)	Batt. recharge time
<b>Vscan (version 1.2) (GE Healthcare)</b>	2D Color Doppler	1.7 to 3.8 Phased array	3.5 inches	390 g	Voice recording	MicroSD	90 min	1 h (90%)
<b>Signos (Signostics)</b>	(2D; transducer arched back and forth) Motion mode	3.5 and 7.5 Single element	3.0 inches	~300 g	Touch pad	MicroSD	60 min	Fully charged 3h 2 h(80%)
<b>MobiUS SP1 (Mobisante)</b>	2D	3.5, 5 (and 7.5) Mechanical, single element	4.1 inches	330 g	Touch screen	8G with MicroSD	60 min (330 with larger battery)	NA
<b>P10 (Siemens)</b>	2D	2 to 4 Phased array	3.7 inches	725 g	Keyboard	SD	100 min	Fully charged 2.5 h 1h (75%)

**Table 2:** 2D: 2D grayscale; Batt.: Battery; NA: Not applicable. Reproduced from (6) with permission from Expert Reviews Ltd.

Figure 3. Comparison of image quality of one pocket-size device and high-end echocardiography.



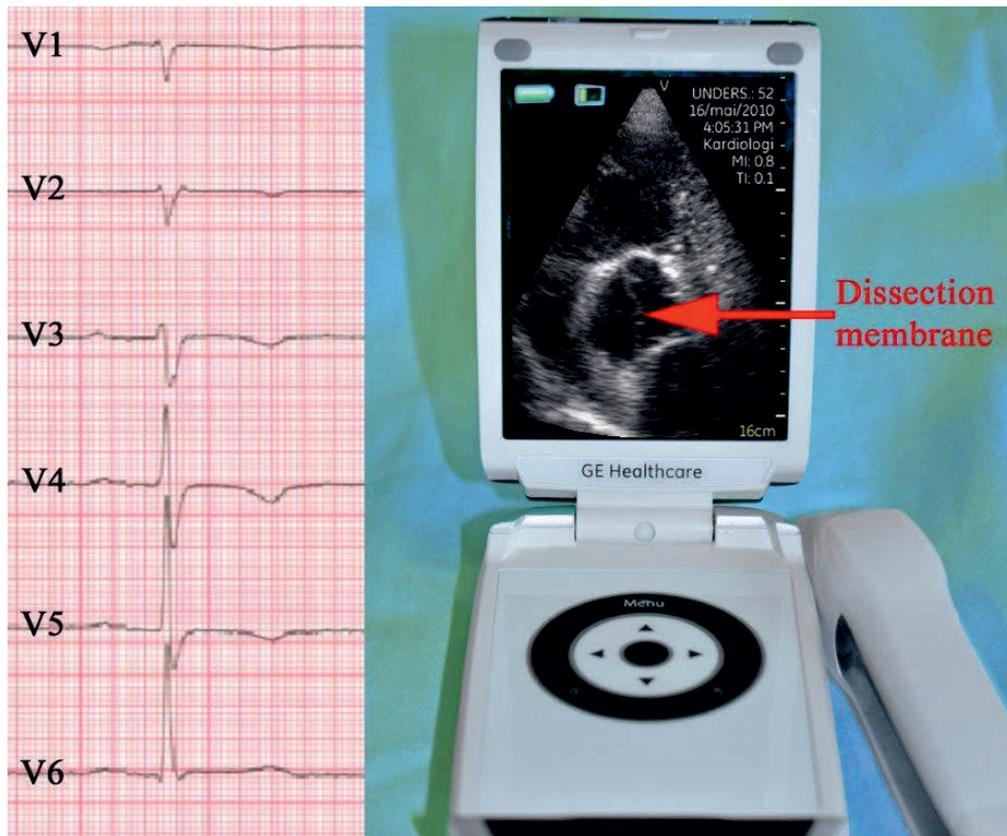
**Figure 3:** Images from GE Healthcare’s Vscan™ device are shown in the top panels and images from a high-end echocardiographic device are shown at the bottom. (A) Echogenic patient. (B) Patient with suboptimal echogenicity. (C) Patient with bad echogenicity. (D) Patient with pericardial effusion. (E) Patient with mitral regurgitation. The pathology is somewhat more easily detected with the wider image sector of the high-end echocardiographic device. Reproduced from (7), with permission from Elsevier.

### 1.3 Point-of-care ultrasound.

Point-of-care ultrasonography is defined as ultrasonography brought to the patient and performed by the provider in real-time (8). This makes it possible for the clinician to correlate

symptoms, clinical findings and sonographic findings without time delay, and thus, increases the diagnostic precision (Figure 4).

Figure 4. Illustration of aortic dissection diagnosed with pocket-size ultrasound.



**Figure 4:** Clinical case of a patient with change in diagnosis after examination with pocket-size ultrasound. A 64-year-old woman was admitted with chest pain and a suspicion of coronary ischemia. Electrocardiogram showed T-wave inversions in precordial leads (left figure). Bedside screening with a pocket-sized device revealed dissection of the ascending aorta (right figure). Reproduced from (9) with permission from Oxford University Press.

In a recent review article, three important situations of point-of-care ultrasound were described. 1) Guidance of procedures, for instance pleural and pericardial drainage, to increase success and decrease complications. 2) Diagnostic assessment, explained as a “limited”, or “goal-directed” examination that aims to provide clinicians with an answer to one or several very specific questions that are important to the actual clinical situation. The FAST (Focused Assessment with Sonography in Trauma) protocol in emergency medicine is a combination of 4 such focused examinations. The search for free intraperitoneal fluid, free fluid in the pelvis, pericardial fluid and/or pleural effusion and FAST was some years later extended also to look for pneumothorax (eFAST) (10, 11). 3) Ultrasound screening or the examination of a specific group. Ultrasound is the method of choice because it is mostly non-invasive and there is a complete lack of ionising radiation. However, this has to be balanced with the disadvantages of screening, such as false positive findings resulting in unnecessary examinations and, in the worst case, the wrong treatment. Screening of the abdominal aorta (AA) is an example from clinical practice (12, 13).

#### **1.4 Training and education**

Ultrasound for diagnostic use has no known side-effects. Most procedures are non-invasive, and it has been used for decades without any epidemiologic evidence of harmful effects (14). However, the quality of the ultrasound examinations is very much related to the skills and competence of the user. Thus, a new concern follows the development of the pocket-size devices. The number of ultrasound examinations will increase and the performing physicians will be less experienced. Therefore, there is a need for studies, guidelines and training programmes to ensure competence, define the benefits of appropriate use and limit unnecessary imaging. In 2002, the American Society of Echocardiography (ASE) published the first guidelines on mobile echocardiography, with respect to the use of laptop-size systems

with advanced functionality (15). Here, they emphasise that these devices do not replace the high-end systems. Their main role is to "augment the physical examination", allowing the more rapid assessment of cardiovascular anatomy, function, and physiology. However, appropriate user-specific training (ASE Level 1 at a minimum) and assumption of responsibility are essential to ensure the most accurate acquisition, interpretation, and use of the data. The recent available pocket-size imaging devices are a major step as they bring bedside ultrasound into daily clinical practice. In 2009, the European Association of Echocardiography (EAE, now known as the European Association of cardiovascular Imaging (EACVI)) published recommendations on the use of pocket-size echocardiography (16). The educational needs of potential users other than cardiologists with expert status in echocardiography were stated. Furthermore, four topics were of major concern: (1) Pocket-size imaging devices do not provide a complete diagnostic echocardiographic examination; (2) imaging assessment with pocket-size imaging devices should be reported as part of the physical examination of the patient; (3) with the exception of cardiologists who are certified for transthoracic echocardiography, specific training and certification is recommended for all users (the certification should be limited to the clinical questions that can potentially be answered by pocket-size devices); and (4) the patient has to be informed that an examination with the current generation of pocket-size imaging devices does not replace a complete echocardiogram.

The level of training required may differ depending on the clinical scenario. To perform a highly focused examination, like assessing a patient with systemic arterial hypertension for left ventricular (LV) hypertrophy, does not require the same level of competence as performing a cardiovascular examination in the emergency room. The competence levels for the different clinical scenarios must be tested out. The entire spectra of users ranges from general practitioners (GPs) working without any ultrasound expertise in

their surroundings, via residents who are cooperating closely with their supervisors, to highly skilled cardiologists without any additional competence requirements.

Subjective judgment is a well-recognised limitation in echocardiography that may increase with less experienced users. The automation of simple quantitative parameters may increase the clinical confidence and may represent an advantage in the use of these devices.

### **1.5 Clinical benefit**

Historically, the introduction of new diagnostic devices into clinical practice has been met with great scepticism; examples include the stethoscope and the ECG. The most important arguments have been the concern of introducing false negative findings and missing important pathology or, in contrast, putting patients through unnecessary diagnostic and potentially harmful examinations because of false positive findings. With respect to pocket-size echocardiography, the false positive findings may represent a burden to the busy echo labs and hospital departments. Thus, in line with all new diagnostic tests or strategies, pocket-size ultrasound should be scientifically evaluated before implementation into daily clinical practice. The sensitivity, specificity and positive and negative predictive values are some of the data of greatest value when evaluating a new diagnostic test (Table 3).

Table 3. Illustration of the terms sensitivity, specificity, positive and negative value.

	<b>Disease - present</b>	<b>Disease - absent</b>
<b>Positive test result</b>	A (True positive)	B (False positive)
<b>Negative test result</b>	C (False negative)	D (True negative)

Sensitivity:  $A/A+C$

Specificity:  $D/D+B$

Positive predictive value:  $A/A+B$

Negative predictive value:  $D/D+C$

## **2 Aims**

### **2.1 General aims**

The increased availability of relatively cheap ultrasound scanners made possible by the development of the recent miniaturised machines have raised an important question: Will non-expert as well as expert users in different clinical scenarios be able to use these devices correctly and increase their diagnostic precision? This important question has been the main issue of this thesis. In the first paper, we studied how GPs could perform a limited echocardiographic examination and assess LV systolic function after a limited training programme. The second paper focused on how an automatic measurement of mitral annular excursion (MAE) can improve this decision making. In the second part of the thesis, we have focused on pocket-size ultrasound as a tool in the emergency room setting: first, with non-experts focusing on reliability and feasibility of pocket-size echocardiography and second, with experts focusing on the diagnostic influence of pocket-size ultrasound.

### **2.2 Specific aims**

- **To assess if GPs were able to evaluate an echocardiographic index of LV function.**
- **To develop a fast, automatic measurement of MAE using a pocket-size ultrasound system.**
- **To study the feasibility and reliability of point-of-care pocket-size echocardiography performed by medical residents.**
- **To assess whether pocket-size ultrasound improves diagnostics in patients admitted to medical departments when used by experts.**

We have performed 4 studies, each published as a separate paper. The 4 studies are discussed separately under the common headings below.

### **3 Materials**

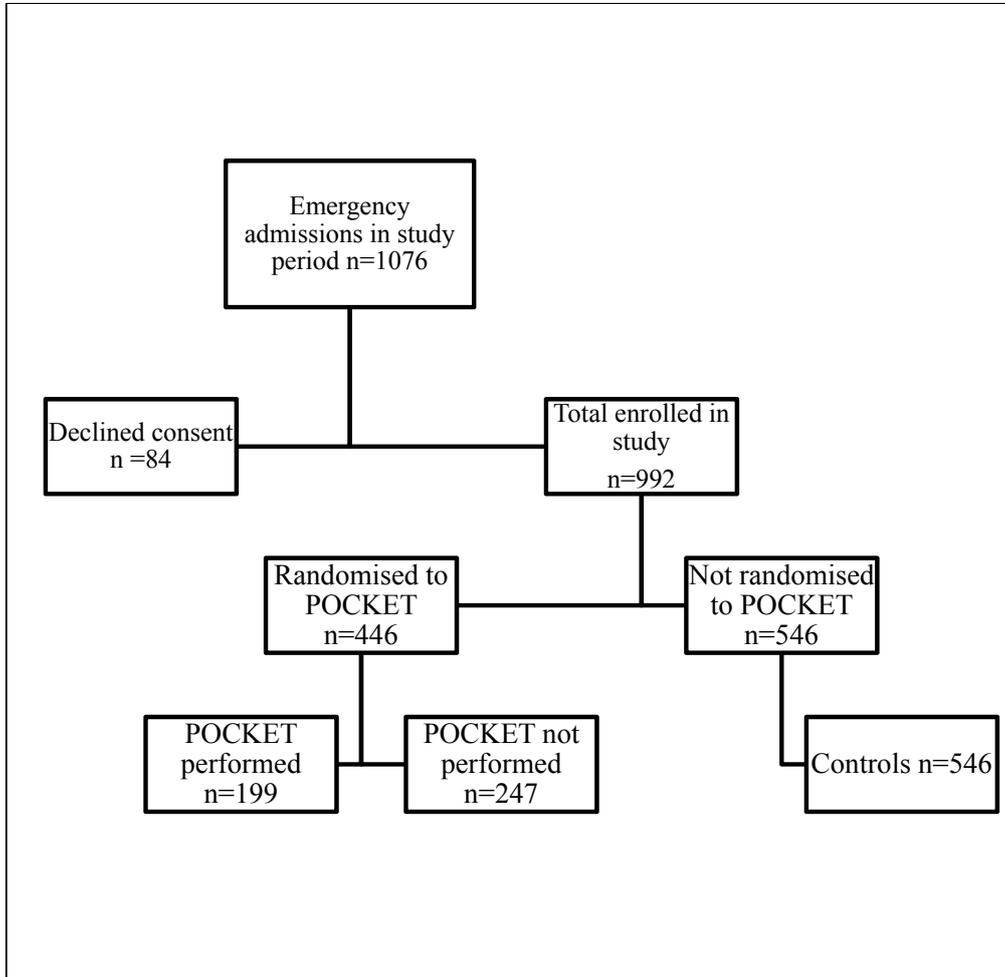
**Study 1:** The study was performed in three different primary care centres in Norway. Seven GPs participated and 92 patients were included: 61 (66%) males, with a median (range) age of 72.5 (38-88) years. Patients with at least one of the following characteristics were recruited by their GPs: Systolic heart failure (32%), earlier myocardial infarction (63%) or arterial hypertension (40%). There were no specific exclusion criteria and no selection according to echogenicity. The 3 different centres included 19, 21 and 52 patients. The different GPs included median (interquartile range) 4 (3-21) patients.

**Study 2:** The first 30 patients from Study 1 were included in this feasibility study focusing on the automatic measurement of the MAE.

**Study 3 and 4:** These studies were performed at the Department of medicine at the non-university Levanger Hospital in Norway. The hospital serves the southern part of Nord-Trøndelag County and has a population of about 100,000. In study 3, 199 patients were included in the period April 4th to June 23rd 2011. The inclusion was performed by 1 of 6 participating residents. At the start of the study, the department had 12 medical residents, and half of them were randomised to participate in the study. During the study, another two residents joined the department, but did not participate in the study. The residents are on-call 24/7; thus, the 6 participating residents covered approximately 42% of the total period of inclusion. The patients were included on the days that these 6 residents were on-call for general medicine. Only patients that did not consent to participate or did not stay long enough in the department to participate were excluded. However, due to logistical reasons, busy

working hours and the residents being informed to place priority on the standard diagnostics and treatment of patients, the inclusion of patients was restricted to 199 of the 446 available patients (Figure 5). In study 4, 196 patients were included in the period from March 1st 2010 to September 30th 2010. The patients were included by 1 of 3 participating cardiologists. The inclusion was restricted to the dates when one of these three was the specialist on call for general medicine. The 3 participating doctors covered 49 ward rounds in the period of inclusion. Only patients admitted to the department early enough to be present on the wards before the specialists' ward round at 5-7 pm were available for inclusion in the study. Table 4 shows the basic characteristics of the participants in the two studies.

Figure 5. Flow chart illustrating inclusion in study 3



**Figure 5:** Flow chart illustrating the study population and randomisation categories.

Table 4. Basic characteristics of the participants in Study 3 and 4.

	199 patients in study 3	196 patients in study 4
	Mean±SD (range)*	Mean±SD (range)*
Age, years	65.6±18.2 (17.1-98.5)	68.1 ± 15.0 (20-95)
Male, N (%)	107 (53.8)	111 (56.6)
Height, cm	170.9±9.7	171.7 ± 9.5
Body mass index, kg/m <sup>2</sup>	26.4±5.6	26.9 ± 5.8
Systolic blood pressure, mm Hg	143.9±28.6	144.6 ± 31.3
Diastolic blood pressure, mm Hg	75.0±15.6	78.7 ± 18.6
Heart rate, bpm	82.8±22.6	80.5 ± 21.6
Atrial fibrillation, N (%)	33 (16.6)	32 (16.3)
Known hypertension, N (%)	67 (33.7)	69 (35.2)
Known diabetes, N (%)	36 (18.1)	32 (16.3)
Known myocardial infarction, N (%)	32 (16.1)	47 (24.0)
Known angina, N (%)	17 (8.5)	36 (18.4)
Known heart failure, N (%)	20 (10.1)	17 (8.7)
Known peripheral vessel disease, N (%)	7 (3.5)	18 (9.2)
Known stroke, N (%)	35 (17.6)	26 (13.3)
Known cardiovascular disease, N (%)	71 (35.7)	91 (46.4)
Known cancer, N (%)	16 (8.0)	16 (8.2)

Table 4: \*Data are presented as mean±SD (range) unless otherwise specified.

## **4 Methods**

### **4.1 Study design**

*Study 1:* A feasibility and reliability study aimed to see whether GPs without experience in echocardiography were able to evaluate the systolic function of the left ventricle (LV) in patients with recognised or at risk of developing heart failure. Pocket-size ultrasound was used and the MAE was assessed as a surrogate marker for LV function.

*Study 2:* A feasibility study assessing a fast, automatic method for measurement of the MAE using pocket-sized ultrasound.

*Study 3 and 4:* In Study 3 we assessed the feasibility and reliability of pocket-size ultrasound examinations when performed by medical residents. Study 4 was a prospective observational study focusing on the diagnostic influence of adding an examination with a pocket-size ultrasound device to standard care. Firstly, patients were admitted to the emergency room and triaged according to their symptoms. Secondly, a resident carefully took a medical history and performed a physical examination. Laboratory testing and diagnostic imaging was done in a normal goal-directed manner. Thus, usual care diagnostics were performed prior to the examination with pocket-size ultrasound device. In study 3, the pocket-size examination was performed by one of the six medical residents taking part in the study. In study 4, the pocket-size ultrasound examinations were performed by three participating cardiologists experienced in abdominal ultrasound and echocardiography. In both studies all patients had standard follow-up according to their symptoms and findings. In study 3, approximately ten negatively described pocket-size ultrasound examinations per resident were referred for reference imaging to better study the specificity of the ultrasound examinations. In study 4, patients admitted to the cardiology department were routinely examined by reference

echocardiography. In both study 3 and 4, relevant diagnostic imaging was performed in all patients where pathology was suggested either by the standard clinical care or by pocket-size ultrasound.

#### **4.2 Education in ultrasound**

**Study 1:** None of the participating GPs had any experience in echocardiography, although all of them had observed demonstrations of echocardiographic examinations. They received a total of 8 hours of supervised training. The lecturer throughout this course was a cardiologist certified in echocardiography in accordance with the requirements specified by the Norwegian Medical Association. In the first 4 hours of the course, the GPs were taught the very basic principles of theoretical echocardiography and anatomy of the heart as visualised by ultrasound. They were taught how to examine the patients positioned in the left lateral decubitus position, and how to make an optimal apical 4-chamber view. They were also taught how to interpret the LV function by measuring the MAE. The next 4 hours consisted of practical training, including practicing on each other and on 3-5 patients. After the supervised training period they had the opportunity to practice with the scanner without supervision for a period of one week before the study started.

**Study 2:** The recordings were performed by a certified cardiologist experienced with the pocket-size device; no other education was provided.

**Study 3 and 4:** In Study 3, the residents went through a brief training program consisting of 4 hours of lectures dealing with the theoretical basics and pitfalls of cardiovascular ultrasonography. Plenty of normal and pathological findings were demonstrated, as well as all residents having access to an in-house virtual ultrasound imaging library. All participating

residents were given a personal supervisor (cardiologist). They then underwent a three month period of practical training, first together with their supervisors and then on their own with close connection to the supervisors, having the opportunity to discuss their findings. They were told to perform at least 100 examinations during the tutorial period and they actually performed a median (interquartile range) of 95 (80-225) examinations. A median (interquartile range) of 33 (20-85) examinations were supervised in real-time. In Study 4, all three internists were certified cardiologists with an EAE advanced competence level in echocardiography (17). They were also experienced in performing abdominal ultrasound; all had performed more than 500 examinations, but none with any formal competence. All internists were familiar with the use of the pocket-size ultrasound device.

### **4.3 Ultrasound imaging**

In all four studies, the point-of-care ultrasound examinations were performed with the pocket-size device Vscan (GE Healthcare, Horten, Norway), which offers B-mode and CF imaging. A phased array probe with a bandwidth of 1.7 to 3.8 MHz was used. This is a true pocket-size device with a total weight of 390 g (scanner-unit and probe). An algorithm enables the automatic storage and looping of a cardiac cycle without an ECG signal (18). All images and recordings were saved on the device's micro-SD. Patient identification was enabled by voice recording and stored as part of each examination.

**Study 1:** All patients were examined in their primary care centres. An examination contained a recording of an apical 4-chamber view recorded with the patient in left lateral decubitus position. In an adjacent examination room, a reference examination was made by a cardiologist certified in echocardiography using a laptop scanner (Vivid I, GE Healthcare, Horten, Norway). The reference examination was performed immediately (< 30 minutes) after

the GP finished his/her examination, and included parasternal long- and short-axis views and apical 4-chamber, 2-chamber and long-axis views in grey scale and colour mode as well as Doppler recordings. Immediately after having performed the complete scan, the cardiologist also examined all patients with the pocket-size scanner in line with the above described protocol.

**Study 2:** In the 30 first patients from Study 1, recordings from both pocket-size and laptop scanners were included in a feasibility study testing an automatic measurement of the MAE. The B-mode apical 4-chamber recordings were used.

**Study 3 and 4:** The pocket-size ultrasound examination was performed with the participants in left lateral decubitus position, as well as in supine position for examination of the abdominal organs and pleural cavity. The cardiovascular examination included parasternal long- and short-axis views and apical 4-chamber, 2-chamber and long-axis views. All views used grey scale and CF modes. Right (RV) and LV function was assessed semi-quantitatively from the apical and parasternal recordings and classified as normal/near normal, moderate dysfunctional or severe dysfunctional. All four valves were examined from the standard views and classified as normal or having calcifications and/or regurgitations. Valvular pathology/dysfunction was classified as mild, moderate or severe. The left atrium (LA) was measured in end-systole on parasternal long axis recordings and classified as normal (< 40 mm), moderately dilated (40-50 mm) and severely dilated (> 50 mm). The inferior vena cava (IVC) was assessed at the end of expiration and inspiration from the sub costal window to estimate right atrial pressure (19). Both pleural cavities were examined and if pleural effusion was present, the amount was quantified as a large or small amount of effusion. A large amount of pleural effusion was stated when the diameter of fluid between the thoracic wall

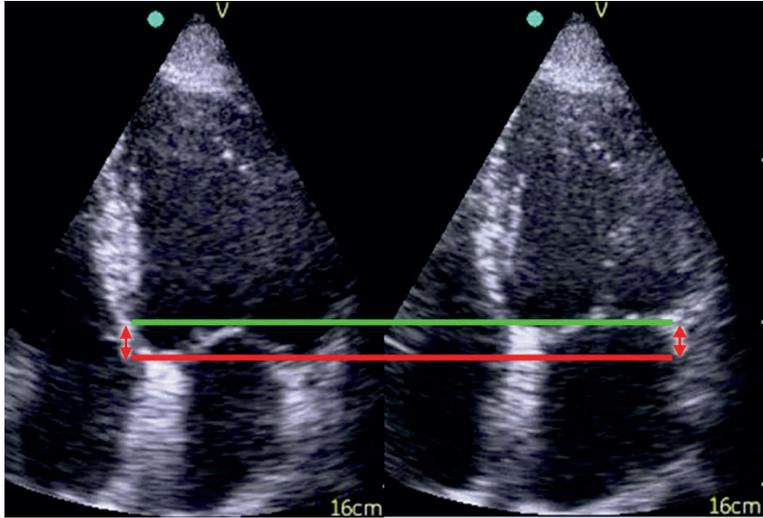
and the lung exceeded 5 and 4.5 cm in the left and the right pleural cavity, respectively. Using the abdominal ultrasound examination, the gallbladder and liver were classified as normal or abnormal, where ultrasound evidence of cholecystitis, cholelithiasis or intrahepatic tumours are examples of abnormal findings. The kidneys were classified as either normal, evidence of hydronephrosis or other pathology. The AA was assessed distally to the bifurcation and classified as normal or aneurysmatic if the maximal diameter exceeded 35 mm in study 3, and if it exceeded 30 mm in study 4. All pathological findings were confirmed by standard diagnostic procedures. Standard echocardiography was performed in the hospital's echo-lab under optimal conditions. The system used was a Vivid 7 scanner (GE Vingmed Ultrasound, Horten, Norway) using a 2.0 MHz phased-array transducer (M3S) with bandwidth 1.5–3.6 MHz. Second harmonic imaging was used and the sector angle set to 90° as default, but was adjusted when appropriate. Storage and looping of cardiac cycles were ECG triggered. The standard examinations were performed independently by one of four experienced cardiologists blinded to the results of pocket-size ultrasound. The same cardiovascular structures as described above were measured and classified according to the guidelines of the EACVI (former EAE) (20-23). LV ejection fraction (LVEF) was measured by Simpson's rule from apical four-chamber and two-chamber views. Dimensions were measured from parasternal recordings. Valvular pathology was quantified according to the recommendations from the EACVI (former EAE) (21, 22). For the analyses in the patients who underwent both echocardiographic and radiologic examinations, the radiologists' quantification of pleural effusion and size of the AA was preferred compared with the echocardiographic measurements.

#### **4.4 Data analysis**

In all studies, the pocket-size ultrasound recordings were transferred to the commercially available software Vscan Gateway (GE Healthcare, Horten, Norway) on a standard laptop PC. The reference examinations performed were exported to the commercially available software EchoPAC PC version BT 09 (GE Vingmed, Horten, Norway).

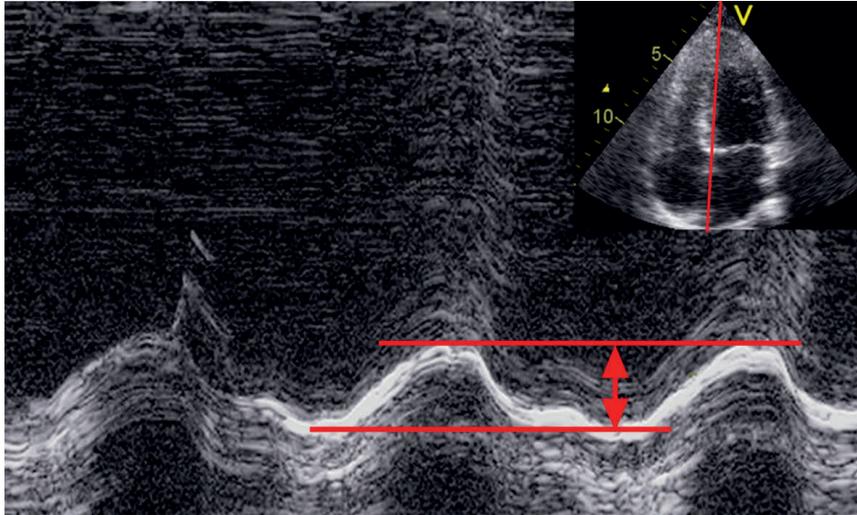
**Study 1:** The MAE was measured by the GP examining the actual patient. It was measured in the loop of one cardiac cycle. The Vscan has a limited field-of-view of 60 degrees for 2D imaging. Due to dropouts and out-of-plane movement of the lateral part of the mitral ring, the septal part was chosen for all measurements. The measurement was made by scrolling the 2D loop from end-diastole to end-systole and then measuring the total displacement of the septal part of the mitral annulus, which represents the total displacement throughout a cardiac cycle (Figure 6). All of the recordings acquired by the GPs were also analysed off-line by an unbiased cardiologist who was certified and experienced in echocardiography. In the reference examination, the M-mode recording of the mitral annulus was measured. The M-mode cursor was aligned parallel to the septum and lateral wall. The systolic excursion was measured from the lowest point at end-diastole to the highest point at end-systole (24) (Figure 7). Only septal measurements were used in the correlations to the pocket-size recordings.

Figure 6. MAE measured on pocket-size scanner.



**Figure 6:** Measurement of the septal MAE in 2D. 2D recording of the LV in end-diastole (left) and end-systole (right). The red line indicates the position of the mitral annular septum in end-diastole and the green line, the position in end-systole. The distance between the lines (red arrows) represents the total distance/excursion by the septal part of the mitral annulus through a complete cardiac cycle. Reproduced from Paper 1, with permission from Oxford University Press.

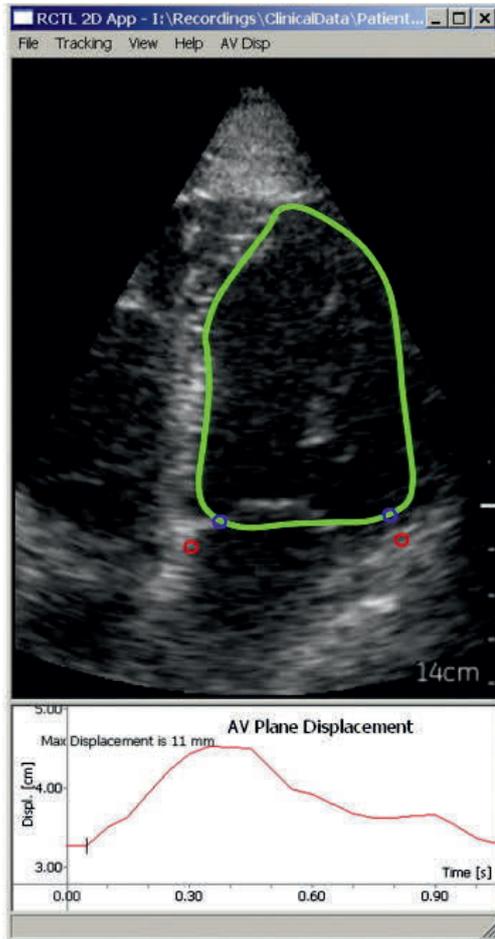
Figure 7. MAE measured on laptop scanner.



**Figure 7:** M-mode registration of septal MAE. The distance between the red lines (arrow) indicates the total distance/excursion of the mitral annular septum through a complete cardiac cycle. Reproduced from Paper 1, with permission from Oxford University Press.

**Study 2:** We tested the feasibility and reliability of an automatic algorithm for MAE estimation. We developed a fully automatic algorithm which combines speckle tracking and Kalman-filter segmentation to make a robust MAE estimate (25-29). The algorithm was tested offline on a standard laptop computer. The algorithm was tested fully automatic. One complete cardiac cycle must be analysed to calculate MAE. In addition, the filter must have converged before initialising the speckle-tracking points; this normally occurs within the first 10 frames. For convenience, each recording was run for two complete cycles. At the end of the second cycle, the MAE value was automatically stored together with an image and movie of the tracking (Figure 8). Only tracking the septal part of the mitral annulus was also tested, as the image quality is generally better on the septal side of the apical four-chamber images.

Figure 8. Example of an automatic tracking of the mitral annulus.



**Figure 8:** An example of automatic tracking of the mitral annulus and measurement of the AV plane displacement or MAE. Reproduced from Paper 2, with permission from Elsevier.

Semiautomatic operation was tested by allowing a second cardiologist, blinded to the reference measurements, to operate the algorithm while allowing for manual corrections. He had the option of making corrections to the initialisation and turning off the lateral tracking point.

**Study 3:** In Study 3, the feasibility and reliability of pocket-size examination performed by medical residents were compared to high-end diagnostics by cardiologist and radiologists.

**Study 4:** In study 4, the diagnostic influence of the pocket-size examinations were studied. Diagnostic corrections were made after the pocket-size ultrasound examination. All patients were discussed in an end-point committee consisting of two residential and one external (St. Olav, Trondheim University Hospital) internists experienced in echocardiography and abdominal ultrasonography. The committee graded the diagnostic usefulness of the bedside pocket-size ultrasound examination into one of the following categories: 1) The principal diagnosis was changed, 2) the principal diagnosis was confirmed, 3) an additional diagnosis important for in hospital or post discharge follow-up, which did not influence the treatment of the principal diagnosis, was made, or 4) the results from the examination with pocket-size device did not have any impact on the actual stay or the follow-up of the patient.

#### **4.5 Statistics**

Statistical analyses in all studies were performed using SPSS PASW Statistics 18.0, 19.0 and 20.0.

**Study 1:** The null hypothesis corresponded to no difference between the MAE measured by GPs and a cardiologist. Continuous values are expressed as median and range. The different measurements were compared using paired t-test and Pearson's  $r$ . Bland-Altman plots and scatter plots were produced (30). Because the differences were normally distributed, we used the paired t-test to compare MAE measured by the GPs and the cardiologist. The coefficient of repeatability and mean error of the MAE was calculated for pocket-size measurements. The

inter-observer coefficient of repeatability was defined as 1.96 SD of the differences in repeated measurements.

**Study 2:** The null hypothesis corresponded to no difference between the automatic method and the manual M-mode reference. The automatic results and the M-mode references were compared using paired t-test and Pearson's  $r$ . Bland-Altman plots and scatter plots of the results were produced. The mean and maximum absolute errors were calculated. To assess the value of user interaction, the results from the semiautomatic analysis were also analysed.

**Study 3 and 4:** The basic characteristics are presented as mean  $\pm$  standard deviation (SD) and range. Spearman's  $r$  was used for comparison of the quantification of pathology between the pocket-size and the high-end diagnostics. Data were presented as  $r$  (95% confidence interval (CI)) with the 95% CI computed using bootstrapping. For the comparison of continuous variables between the pocket-size and the high-end examinations, Pearson's  $r$  was used. In study 4, logistic regression analyses was used to study predictors for diagnostic influence of the ultrasound examinations; change of primary diagnosis or any diagnostic usefulness assessed (change or verification of primary diagnosis, or an important additional diagnosis) were used as the dependent variable, and age and risk factors were included as independent variables. In these analyses, age was entered as a continuous variable.

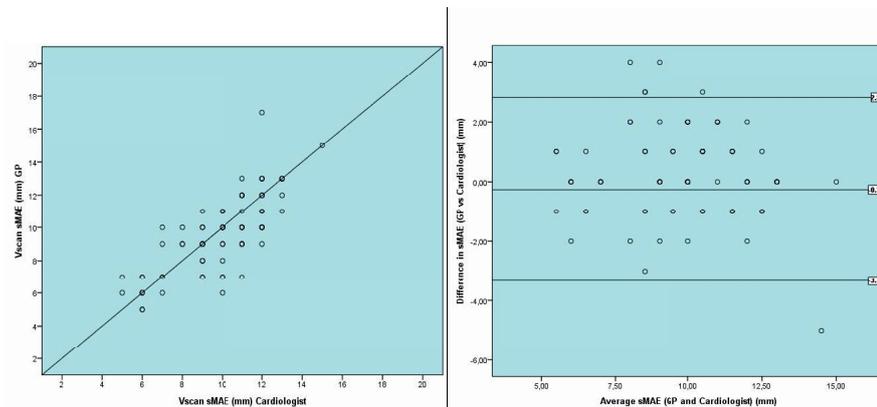
#### **4.6 Ethics**

All of the studies were approved by the Regional Committee for Medical Research Ethics, and conducted according to the second Helsinki Declaration. All patients gave their written informed consent to participate.

## 5 Summary of results

**Study 1:** In 80 (87%) patients, the GPs were able to obtain a 4 chamber view of such a quality that they were able to measure the MAE as an index of LV systolic function. Seven of the remaining recordings were of such a bad quality that further analysis was impossible and an image was recorded instead of a video loop in 5 of the recordings. The pocket-size examination was performed in less than 5 minutes. Comparing the measurement of the MAEs made by the GPs and the MAEs made by the cardiologist, both using the pocket-size device, the Spearman's  $r$  was 0.78, 95% CI (0.67-0.86),  $p < 0.001$  and the 95% limit of agreement was  $-0.26 \pm 3.02$  mm (Figure 9).

Figure 9. Correlation and agreement of GP's measurement of septal MAE compared to reference method



**Figure 9:** Spearman's rank correlation (left) and the Bland-Altman plot illustrating the 95% limits of agreement (right) between measurements of septal MAE with pocket-size ultrasound (Vscan) performed by the GPs compared to the cardiologist. The Bland-Altman plot is reproduced from Paper 1, with permission from Oxford University Press.

When a second cardiologist did the off-line analysis on the recordings acquired by the GPs, the Spearman's  $r$  was 0.82 (0.72-0.90),  $p < 0.001$  and the 95% limit of agreement was  $-0.51 \pm$

2.68 mm. Comparing septal MAE by two different scanners, operated and interpreted by one cardiologist, there was an excellent correlation  $r = 0.89$  (0.81-0.94),  $p < 0.001$  with a 95% limit of agreement  $0.11 \pm 1.98$  mm.

There were no significant differences in measurements of septal MAE, neither between the different operators or the different scanners. When analysing the same measurements for each of the 3 centres, we did not find any significant differences (Table 5).

Table 5: Differences between scanners and different operators

	<b>Total n=92</b>	<b>Centre 1 n=21</b>	<b>Centre 2 n=52</b>	<b>Centre 3 n=19</b>
<b>Pocket-size GP vs. Laptop*</b>	-0.15 mm (-0.60-0.30)	0.77 mm $\pm 1.56$	-0.73 mm $\pm 1.96$	1.18 mm $\pm 2.09$
<b>Pocket-size GP /cardiologist vs. Laptop*</b>	0.08 mm (-0.29-0.44)	0.65 mm $\pm 1.32$	-0.24 mm $\pm 1.68$	0.64 mm $\pm 1.43$
<b>Pocket-size cardiologist vs. Laptop*</b>	0.11 mm (-0.10-0.32)	0.57 mm $\pm 1.29$	-0.09 mm $\pm 0.93$	0.19 mm $\pm 0.66$
<b>Pocket-size GP vs. Pocket-size cardiologist**</b>	-0.26 mm $\pm 3.02$	0.12 mm $\pm 1.41$	-0.65 mm $\pm 1.37$	1.0 mm $\pm 1.79$
<b>Pocket-size GP /cardiologist vs. Pocket-size cardiologist **</b>	-0.05 mm $\pm 2.68$	0.00 mm $\pm 1.50$	-0.18 mm $\pm 1.38$	0.45 mm $\pm 1.04$

\* Data are mean difference and 95% CI for the total population and mean difference  $\pm$  SD for each centre.

\*\* Data are mean difference and 95% limits of agreement for the total population and mean difference  $\pm$  SD for each centre.

**Table 5:** Showing the mean difference and the 95% limit of agreement for the different comparisons for the total population and for each of the 3 centres. Abbreviations: Pocket-size GP; Pocket-size ultrasound performed and analysed by the general practitioner. Pocket-size cardiologist; Pocket-size ultrasound performed and analysed by the cardiologist. Pocket-size GP/cardiologist; Pocket-size ultrasound performed by the general practitioner and analysed by the second cardiologist. Laptop; Echocardiography performed and analysed by the cardiologist using a laptop scanner. Reproduced from Paper 1, with permission from Oxford University Press.

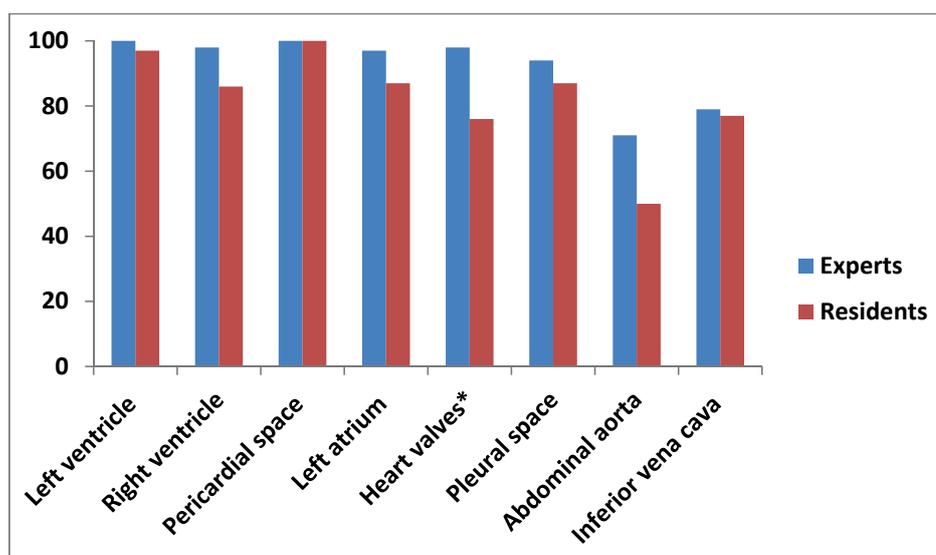
Sensitivity and specificity of GP operated pocket-size device to detect a reduced LV function, defined as a septal MAE < 10 mm measured by the cardiologist with a pocket-size scanner, was 82.2% and 76.9%, respectively. The negative and positive predictive value was 86.6% and 66.7%, respectively. When the offline analysis of GP recordings was performed by the second cardiologist, sensitivity and specificity increased to 86.0% and 82.8%, respectively, and the negative and positive predictive value increased to 91.3% and 73.5%, respectively.

**Study 2:** The automatic algorithm was tested using 30 pocket-size apical four-chamber recordings made by a cardiologist, who also did the reference measurements. Comparing the results from the automatic algorithm with the anatomic M-mode reference measurements, the Spearman's  $r$  was 0.62,  $p < 0.001$  and the 95% limits of agreement were  $-1.80 \pm 1.96$  mm when both the lateral and septal side of the mitral annulus were tracked. When only the septal position was tracked, Spearman's  $r$  was 0.61 and the 95% limits of agreement  $-0.27 \pm 1.89$  mm. When allowing for manual interaction, 50% of the recordings were processed fully automatic. The most common corrections were re-initialisation of tracking points and/or disabling the lateral point. The 95% limits of agreement were then reduced to  $-1.57 \pm 1.72$  mm and Spearman's  $r$  increased to 0.69,  $p < 0.001$ . The standard deviation was less than 2.0 mm, which should be considered acceptable given the image quality and number of patients included in the study. The results suggest that the algorithm measures MAE using pocket-size data with accuracy suitable for rapid assessment of LV systolic performance.

**Study 3 and 4:** In Study 3, the total time used for the ultrasound examinations was  $11.5 \pm 4.3$  min:  $6.1 \pm 2.7$  min for the cardiovascular examination and  $5.4 \pm 2.7$  min for the focused abdominal examination. In Study 4, the total time used for the ultrasound examinations was

6.8 ± 2.0 min: 4.3 ± 1.6 min for the cardiovascular examination and 2.5 ± 1.0 min for the focused abdominal examination. Figure 10 shows the percentage feasibility defined as the ability to record and interpret different cardiovascular structures from the two studies.

Figure 10. Feasibility of cardiovascular structures in study 3 and 4.

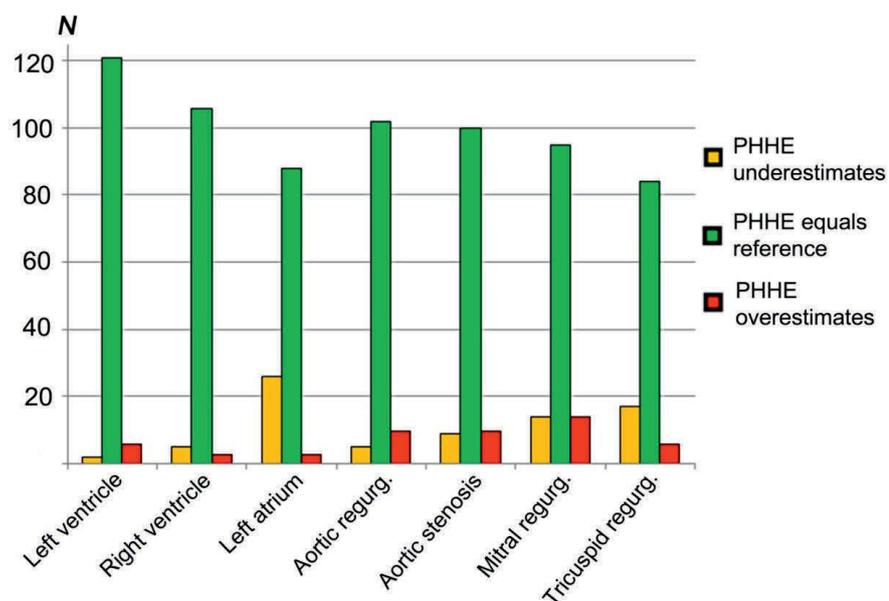


**Figure 10:** Feasibility (%) of different cardiovascular structures by pocket-size echocardiography when the examination was performed by experts and residents. \*All 4 valves in by the experts, and all except the pulmonic valve in the resident study.

The LV was assessed to satisfaction in more than 97% in both studies and the pericardium in all patients. The aortic and atrioventricular valves were assessed in at least 76% by the residents and the pulmonary valve in less than 50% of the patients. Among the experts, all valves were assessed in at least 98%. The AA was completely assessed in 72% and 50% of the participants when examined by experts and residents, respectively. The experts assessed the IVC in 84%. The correlation of pocket-size echocardiography and high-end echocardiography when performed by experts was  $r \geq 0.85$  for quantification of LV regional

function, LV and RV global function, valvular function, pleural- or pericardial effusion and detection of abdominal aortic aneurysms. LA size and IVC dimensions showed correlations of  $r = 0.65$  and  $r = 0.68$ , respectively. Sensitivity and specificity of pocket-size ultrasound examination with respect to detect at least moderate dilatation of LA were 0.81 and 0.68, respectively, whilst data for all other presented indices were  $\geq 0.88$ . When performed by the residents, global LV function and pleural and pericardial effusion showed very strong correlation with standard diagnostic procedures (Spearman's  $r \geq 0.83$ ). Regional LV dysfunction correlated moderately ( $r = 0.60$ ). Quantification of aortic valve calcification/stenosis and regurgitation showed strong correlation with  $r = 0.67$  and  $r = 0.68$ , respectively. Quantification of regurgitations in the atrioventricular valves showed moderate correlations:  $r = 0.53$  for mitral and  $r = 0.61$  for tricuspid regurgitation, which were similar to quantification of the degree of dilatation of the LA ( $r = 0.61$ ). No serious findings were missed. In detecting an aortic aneurysm, pocket-size measurements correlated to standard diagnostics with  $r = 0.70$ . The diameter of the IVC correlated only moderate with high-end echocardiography, Pearson's  $r = 0.45$ . Figure 11 illustrates the residents' grade of misclassification of ventricular and valvular pathology by pocket-size compared to reference. Table 5 shows sensitivity, specificity, and positive and negative predictive values of the pocket-size devices to detect at least moderate pathology when operated by residents. There was high specificity and negative predictive values of detecting LV and RV dysfunction and aortic valve pathology. Contradictory low sensitivity and low positive predictive values for assessment of RV function and LA size are mainly caused by some underestimation of pathology.

Figure 11. Classification of assessment of ventricular and valvular pathology by pocket-size hand-held echocardiography (PHHE) performed by residents compared to reference echocardiography.



**Figure 11:** Figure illustrates the agreement between PHHE and reference echocardiography in grading of ventricular and valvular pathology. Abbreviations: N, numbers; PHHE; pocket-size hand-held echocardiography; regurg, regurgitation. Reproduced from Paper 3, with permission from Oxford University Press.

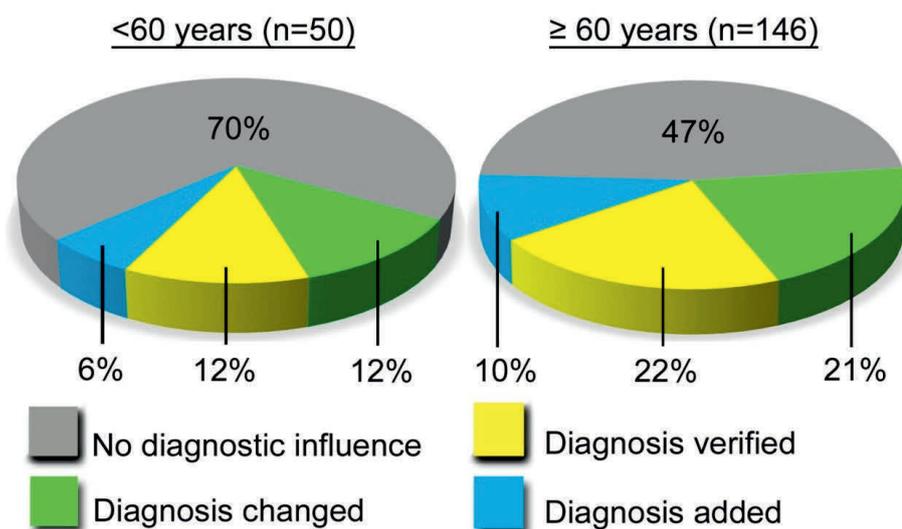
Table 6: Sensitivity, specificity, positive and negative predictive values for detection of at least moderate pathology by pocket-size echocardiography by residents.

	N total	N pathology	Sensitivity	Specificity	PPV	NPV
LV dysfunction	129	30	92	94	80	98
RV dysfunction	115	10	40	97	57	94
LA enlargement	117	68	62	94	93	64
Aortic regurgitation	117	27	82	89	69	94
Aortic stenosis/calcification	119	37	76	88	74	89
Mitral regurgitation	123	48	71	81	71	81
Tricuspid regurgitation	107	49	65	90	84	75

**Table 6:** LV, left ventricle; RV, right ventricle; LA, left atrium; PPV, positive predictive value; NPV, negative predictive value. Reproduced from Paper 3, with permission from Oxford University Press.

The main issue of Study 4 was the clinical influence of routinely adding a pocket-size ultrasound examination (Figure 12). In total, 36 (18%) participants had the main diagnosis changed after the pocket-size ultrasound examination compared to the principal diagnosis based on usual care diagnostics. The principal diagnosis was verified in 38 (19%) patients. An additional important diagnosis without influence on the current stay was made in 18 (9%) patients. In 104 (53%) patients, the pocket-size ultrasound examination did not have any influence on the actual stay or the follow-up of the patients (Figure 12).

Figure 12. Diagnostic usefulness of routinely adding cardiovascular and focused abdominal ultrasound examination.



**Figure 12:** The diagram shows increased diagnostic influence of additional ultrasound examination among those at older age. Reproduced from Paper 4, with permission from Elsevier.

When evaluating predictors of diagnostic influence, the odds ratio (OR) (95% CI) for any diagnostic usefulness (defined as the above categories 1, 2 and 3) was 1.6 (1.3–2.0) per 10 years higher age ( $p < 0.001$ ) and 2.0 (1.7–2.3) ( $p = 0.02$ ) for those with known cardiovascular disease.

## **6 Discussion**

### **6.1 *Physical examination, limitation and medical errors***

Despite the heavy arsenal of diagnostic modalities available in hospitals, autopsies have revealed major diagnostic errors in 30% of cases (31, 32). Thus, there is a need for improvements in diagnostic accuracy. Morgagni (1682–1771) is classified as the founder of the modern physical examination and showed for the first time pathologic changes in human organs induced by diseases (33). The main role of the physical examination is to detect the signs of disease bedside without time delay. In 1816, the French physician Laënnec (1781-1826) revolutionised physical examination by inventing the stethoscope (34). He established the art of auscultation of the chest. Today, the stethoscope is still a mandatory part of the clinical examination, but we have reached new heights due to an impressive amount of research and technology. Ultrasound has become one of the most widely used diagnostic techniques in clinical medicine (23). In parallel to the development of new technologies, the clinical and auscultatory skills of doctors may have decreased (35-37). Mangione and Nieman demonstrated that internal medicine and family practice trainees had a disturbingly low identification rate for important and commonly encountered cardiac events (38) and several clinical conditions are difficult to recognise with physical examination alone, but easy to recognise with ultrasound; examples are pericardial effusion and early LV dysfunction (39). It is of huge importance to identify such conditions early. Including the pocket-size ultrasound device in the physical examination allows for bedside early identification of several diseases (40-43). An early aetiological diagnosis will provide the best patient management and medical errors may be decreased. It may also improve in-hospital workflow (44).

## **6.2 Training and education**

Most of the echocardiographic examinations in the clinical setting have to date been performed with “high-end” systems in echo laboratories. The operators have been experts, such as cardiologists or highly skilled sonographers. This has been the most appropriate way, since the devices have become very advanced and require expertise far above what every physician may achieve. This means that the clinical indication must be recognised by the physician, and the examination must be considered appropriate. The development of pocket-size, easy to handle and inexpensive devices may change this scenario.

In most of the world, a high-end echocardiographic examination is not possible to achieve and, even in the developed world, there is a gap between the capacity and the need for echocardiography and ultrasound in general (45). The important question is therefore in what way the pocket-size devices may bridge the gap, in some situations performed by expert sonographers and in others by the entire scale of non-experts.

It is important to differ between a “gold-standard” device and an “add-on” device when introducing new technology. Pocket-size ultrasound surely represents an “add-on” device. It is technically very simple compared to the high-end machines which should be the choice when dealing with complex cardiovascular pathology. The recommendations from the EACVI (former EAE) emphasise that these devices do not allow for a complete echocardiographic study, but they should augment the physical examination (16). Based on the fact that the pocket-size devices lack advanced functionality, this is a natural conclusion. In recent years, many papers have shown that that the outcome of echocardiographic examinations is very user-dependent (46-50). However, all of the above-mentioned papers demonstrate that a quick focused assessment of cardiac and non-cardiac structures both with experienced and inexperienced users add important information to standard diagnostics and improve diagnostic accuracy. In medical school, it represents an excellent educational tool for

medical students demonstrating both normal organs and pathological findings in an excellent way. DeCara et al. demonstrated that 4th year medical students made a far more accurate bedside diagnosis when augmenting their physical examination with a focused pocket-size examination, and in the Wayne State University School of Medicine, Rao et al. demonstrated that first year medical students were very satisfied with an integrated ultrasound curriculum (51, 52). Prinz et al. showed that inexperienced users improved their skills with respect to both image acquisition and interpretation over a few weeks with targeted training (50). Among the trainees, Galderisi et al. demonstrated an additional value of pocket-size ultrasound compared to the physical examination alone, but lower specificity and sensitivity in comparison to experts (53). We do not know the definite level of competence necessary to handle these devices and it may vary according to the clinical scenario. A major goal must be to make the next generation of medical doctors more familiar with the use of point-of-care echocardiography. This may expand the use of ultrasound outside of the echo laboratories and into new arenas, with GP offices representing an important example.

### **6.3 Feasibility and reliability**

The Siemens Acuson P10 and Vscan from GE Healthcare are the two most studied scanners. Several studies have focused on the feasibility and reliability of these scanners, mostly when used by experts. Fukuda et al. showed 100% feasibility and excellent correlation and agreement ( $r = 0.87-0.98$ , all  $P < 0.001$ ) between the Siemens Acuson P10 and a high-end scanner for the measurements of cardiac chamber size and function (LV diastolic and systolic dimensions, fractional shortening, the thickness of the interventricular septum and of the posterior wall, LA dimension and ascending aorta diameter) in 125 unselected patients (54). Kimura et al. used the same scanner in an in-hospital setting and ultrasound experts were shown to be well qualified for assessment and interpretation of LV systolic function and LA

diameter (55). Culp and colleagues have in 2 different studies shown that both expert and novice echocardiographers can use the Siemens Acuson P10 to quantify LVEF over a broad range of patients, and that novice echocardiographers can use the same scanner to estimate the LVEF with fair correlation to standard diagnostics in intubated patients (56, 57). Since the release of Vscan (GE Vingmed Ultrasound) in October 2009, several feasibility studies have been published. Prinz et al. demonstrated negligible deviations between Vscan and a high-end scanner assessing LVEF ( $r = 0.91$ ) and LV measurements ( $r = 0.99$ ); no pericardial effusion or valve stenosis was missed, but regurgitations were slightly overestimated (7). The same group later showed moderate to very high correlations with reference echocardiography when experienced echocardiographers were assessing basic cardiac morphology and function on images obtained using Vscan (58). Galderisi and his group studied 304 consecutive non-cardiologic outpatients; 102 patients were scanned by experts and 202 by trainees. The overall correlation coefficient of examinations performed by Vscan and the high-end device was 0.67 in the pooled population (0.84 by experts and 0.58 by trainees), and importantly, there was a suboptimal precision for trainees in the eyeball evaluation of LVEF, LA dilation and RV dilatation (53). Lafitte et al. showed that Vscan appeared as good as standard full feature echocardiograph in regard to basic and qualitative diagnostic capability. A semi-quantitative visual analysis proved good concordance to conventional quantitative evaluation by a standard examination (59). Our research group showed similar results in a feasibility study, including excellent feasibility for cardiac structures and pleura, which was assessed to satisfaction in at least 94% of patients. Lower feasibility (71-79%) was seen for the abdominal great vessels. Correlations between Vscan and high-end scanner for the assessment of LV function, AA size and presence of pericardial effusion were almost perfect, with  $r \geq 0.92$ . Strong correlations ( $r \geq 0.81$ ) was shown for RV and valvular function, except for grading of aortic stenosis ( $r = 0.62$ ). The correlations were strong for the assessment of IVC and LA

dimensions (60). Thus, in line with recent publications, it may be concluded that most cardiovascular indices may be feasibly and precisely assessed by pocket-size devices, but it is important to state that they shall not serve as a tool for complete echocardiograms. No studies have compared the different pocket-size devices.

#### **6.4 Ultrasound imaging**

Introducing pocket-size devices with a limited range of functionality require that we evaluate the way in which we assess the different cardiovascular structures.

*LV size and function:* All available studies show very strong correlations between pocket-size and high-end diagnostics dealing with LV size and wall thickness. The established way of assessing LV systolic function is LVEF by Simpson's rule from apical four-chamber and two-chamber views. This requires good image quality to correctly detect the endocardial borders. MAE most often assessed by M-mode is related to LVEF (24, 61-65). The MAE is an established and valuable tool for the early detection of reduced LV function and it is easy to obtain even in patients with reduced image quality (65). In our feasibility study (Study 1), we have shown that GPs are able to measure MAE with pocket-size ultrasound and do well compared to an expert. In Study 2, we showed that an automatic algorithm, which it is possible to include and run in real-time in a pocket-size device, may help us to differentiate between normal and abnormal ventricles. However, in a patient with suspected heart failure, the exact cause of the reduced MAE should be assessed further with a full echocardiographic examination in the hands of experts. "Eye-ball" assessment of LVEF and semi-quantitative assessment of LV systolic function is another way to assess LV function, and in Studies 3 and 4 we showed strong correlation to high-end diagnostics, but assessment of EF requires better image quality compared to assessment of MAE.

*Valvular pathology:* Because of the lack of spectral Doppler, valvular morphology, stenosis and regurgitations must be classified semi-quantitatively (21, 22). In our studies, quantification of stenosis was based on the degree of calcification and movement of the cusps/leaflets, while grading of regurgitations was based on the CF signal and size and function of the adjacent chambers, i.e. no mitral regurgitation was graded as severe if the LA size was normal. This is a simplified assessment compared to the high-end examination including spectral Doppler, but all of the mentioned studies show strong to very strong correlations depending on the skills of the sonographer. However, several studies have shown an overestimation of regurgitations due to a sensitive colour Doppler (7, 60) and a trend towards underestimation of, but not missing, aortic stenosis due to the lack of spectral Doppler (7, 60).

*LA enlargement:* Both Studies 3 and 4 showed a moderate correlation of LA dilatation compared to high-end diagnostics. The main explanations of inaccurate measurements in LA size are the timing of measurements made by visual assessment only, and the lack of M-mode and ECG timing on the device.

*The AA:* By definition, an aneurysm of the AA is present when the infrarenal aortic diameter exceeds 3.0 cm (12, 66). However, different studies have used a diameter between 25 and 35 mm as the cut-off for an aneurysm. In Study 3, we used 30 mm as a cut-off. In an attempt to avoid creating diagnoses not important for follow-up of the patients, we changed this to 35 mm in Study 4. In general, we found lower feasibility for AA in both of our studies compared to others (67). The fact that the patients were non-fasting may have reduced abdominal image quality. In Study 3, the residents did not register the aorta as assessed unless the entire length of the aorta was assessed to satisfaction; BMI was approximately 2 kg/m<sup>2</sup> higher in those where the AA was not assessed ( $p < 0.001$ ).

*The IVC:* Both Studies 3 and 4 showed only moderate correlations of pocket-size measurements with high-end diagnostic measurements. The presented data are in line with others (7, 53). This may be related to the timing of measurements in the respiratory cycles, lack of M-mode, which may lead to inaccurate measurements, and the time delay of median 17 and 21 hours between the pocket-size ultrasound examination and the high-end reference echocardiography. Due to physiological variation and any treatment given to the patients during this period, correlations are difficult to make and probably incorrect (19).

## **6.5 Focused echocardiographic examination**

Ultrasonography performed bedside (point-of-care ultrasonography) by the clinicians can provide rapidly available images as an adjunct to clinical findings. This may decrease medical errors if the image quality and interpretation is adequate (8). As described by Moore and Copel there are 3 situations of point-of-care ultrasound; procedural, diagnostic, and screening applications.

Our studies have all been examples of diagnostic assessment or “goal-directed” examinations. First, we showed that it is possible for GPs, after a limited period of focused training, to use a pocket-size ultrasound scanner to assess global LV function in 87% of the patients with or at risk of developing reduced LV function. We know from several studies that GPs have limited tools available for rapid assessment of patients with dyspnoea (68, 69). Martin et al. screened medical inpatient with pocket-size ultrasound and showed that asymptomatic LV systolic dysfunction was present in about 1 of every 20 with at least one risk factor for heart failure (70). We know that treatment of asymptomatic LV systolic dysfunction may reduce morbidity (71). Lipczynska et al. demonstrated that a simplified pocket-size ultrasound examination, performed by an internist with basic training in

echocardiography, yields significant prognostic information in a community cohort of patients with heart failure and/or heart failure risk factors independent of NT-pro-BNP levels (72). In another study, Kajimoto et al. demonstrated that ultrasound examination of the lungs, LV function and IVC represents a very accurate method of differentiating heart failure from pulmonary disease in patients with acute dyspnoea (73). Furthermore, a former study showed that a hand-held device could be reliably used to assess LV hypertrophy in patients diagnosed with arterial hypertension (74); this was also demonstrated using the Vscan (75). These are examples of easy point-of-care examinations with a very limited focus. These scenarios are examples of how point-of-care ultrasound examinations can help to obtain important information in the diagnostics and follow-up of large groups of patients and the fact that focused examinations requires less education and training than a more “complete” examination. As we showed in Study 2, automatic measurements may be added to make these applications even more reliable and easier to perform (76, 77).

Studies 3 and 4 were both examples of a more complete examination, or combinations of focused examinations. Patients admitted to the medical department were examined with pocket-size ultrasound independently of their clinical situation. In Study 4, the examinations were performed by experts and thus, there was no need for further training; the major difference to a reference examination is the limited functionality of pocket-size devices. When performed by residents, the lack of clinical experience and ultrasound knowledge also represents major differences compared to standard care. The recommendations from the EACVI (former EAE) emphasise that this must be reported as part of the physical examination and that the patients must be informed that this does not represent a full echocardiographic study (16). We showed the correct assessment of cardiac and abdominal structures' size and function and a considerable clinical benefit (60).

It is important to emphasise that we are still talking about the physical examination, but that this undoubtedly represents an important step in increasing the yield of the physical examination. We showed that the principal diagnosis, and thereby the treatment, was significantly corrected in nearly 1 in 5 (18%) of patients. Additionally, 20% had their primary diagnosis verified and an additional diagnosis of certain importance was made in 9%. The clinical benefit increased with age, probably illustrating the increased amount of pathology in the older age groups. The total time spent was a mean of 6.8 minutes. Similar studies have been performed by other groups, mainly focusing on feasibility and reliability (7, 53-55, 58, 59, 78-80). With non-expert users, some kind of uncertainty will be introduced. The worst medical scenarios are the false negative findings – another scenario is referring too many patients to the echo lab or to advanced radiological examinations because of false positive findings. In non-expert users, education and a goal-directed training period is mandatory and pocket-size devices should only be used for focused examinations depending on the skills of the user.

## **6.6 Clinical benefit**

All the above mentioned studies show that the pocket-size devices allow for fast and reliable information. The two main concerns are the false negative and false positive findings, in particular with less experienced users. The positive and negative predictive values, sensitivity and specificity are high for nearly all cardiovascular structures when examinations are performed by experts. In particular, no important findings were missed. In Study 3, where residents performed the examinations, the corresponding values were in general lower, but in particular the specificity and the negative predictive values were high (> 80%) for all structures except LA enlargement and tricuspid regurgitation. The presented studies are in line with others (53). A pocket-size scan is an “add-on” to our physical examination and its value

must be interpreted in the context of the specific clinical situation. When performed by experts it contributes positively to the diagnostic process. It establishes a correct diagnosis earlier (Figure 12) – which means immediate referral to the correct department, and establishment of necessary treatment without delay. In some situations it may allow earlier discharge from the hospital. The feasibility and accuracy numbers from the expert studies (Figure 10) should also indicate that a fast pocket-size examination can make a high-end echo study unnecessary in many cases. Cardim et al. showed this in an outpatient clinic reducing the referral rate to high-end echo from 50.3% to 33.9% when standard care was supplemented with a pocket-size scan. When performed by non-experts, the additional value of a pocket-size scan is in general lower, but still it represents a significant add-on value to the physical examination.

Neither our studies nor those of others have provided cost-effectiveness data. These are complex analyses that require several different factors. Examples are the price of a missed diagnosis in a hospital admission, the benefit of an earlier correct diagnosis and the savings associated with reducing the amount of high-end echocardiographic examinations. These studies should be performed in the future.

## **6.7 Automation**

The subjective assessment is a well-recognised limitation in echocardiography that may increase with less experienced users. In this thesis, an automatic algorithm for measuring the displacement of the mitral annulus has been tested. Tracking of the lateral point was the most challenging. The poor lateral tracking is probably caused by inferior image quality on the lateral side and limited sector size, resulting in dropouts and out-of-plane motion. When the average of the septal and lateral excursions was used to calculate MAE, the lateral point introduced a negative bias of 1.8 mm. By tracking the septal points only, the negative bias

was reduced to 0.27 mm. This is in line with former studies assessing the automation of MAE (81). When the algorithm was operated semi-automatically, only 50% of the pocket-size data were processed without human interaction. In most cases, the interactions were disabling of the lateral point and/or re-initialisation of the tracking points. Judging from the results, the main effect of the manual interaction was reduced maximal errors. Another paper from our group demonstrated a similar algorithm aimed to measure the end-diastolic diameter of the interventricular septum (76). This represents a valuable tool in evaluating patients for LV hypertrophy which is of absolute value in the follow-up a patient with arterial hypertension. Furthermore, to aid non-expert users in capturing an apical 4-chamber view, a real-time scan assistant was developed. It showed improved image quality when trialled among medical students using a high-end scanner (82).

Automation of simple quantitative parameters may increase the clinical confidence, in particular in a point-of-care setting among less-experienced users.

## **6.8 Diagnostic impact**

**Study 1:** With tailored training, GPs in this study were able to assess LV function with MAE and a pocket-size device. This may be an important supplement to the physical examination and may become an important tool in evaluating patients with i.e. dyspnoea.

**Study 2:** A fully automatic algorithm for MAE measurement with an accuracy that should be suitable for successfully separating poor ventricles from normal ones was developed.

**Study 3:** By adding a point-of-care pocket-size examination lasting less than 6 minutes, medical residents were able to obtain reliable information of important cardiac structures in

patients admitted to a medical department. Thus, a focused examination performed by residents after a training period have the potential to improve in-hospital diagnostics.

**Study 4:** By adding a cardiovascular and focused abdominal ultrasound examination of mean 6.8 min by pocket-size ultrasound, expert users correctly assessed cardiac and abdominal structure sizes and functions enabling correction of the diagnosis in nearly 1 of 5 patients admitted to a general medical department.

## **7 Limitations**

All of our studies were performed at single or few centres with a limited number of patients. In Study 1, 90 patients resulted in power > 90% at the 5% significance level for detecting a difference in 2 mm (assumed to represent a clinical significant difference) in MAE, assuming one standard deviation (SD) of 1.51 mm. Study 2 was a pilot study and no power estimate was done. In Studies 3 and 4, we aimed for 200 pocket-size recordings, resulting in power > 80% to detect correction of the diagnosis in 6-10% of cases. Patients were selected solely on the days where the participating doctors were on call. In Study 3, only 199 of 446 of the patients randomised to examinations by the pocket-size devices were actually examined (Figure 5). This is mainly explained by busy working hours, hospital logistics and the residents being informed to prioritise standard diagnostics and treatment of patients, but may represent a selection bias.

In Studies 1 and 2, MAE was used as a marker for LV systolic function; in Study 1 this was measured manually by the GP and in Study 2 this was estimated by an automatic algorithm. It is important to specify that MAE only represents a surrogate marker for LV systolic function. Previous studies have shown that MAE not only relates to systolic function, but also those with more compromised diastolic performance had lower MAE (62). MAE is

often measured in several projections, and the MAE value is reported as the average excursion (83). In this work, only the apical four-chamber was used. In Study 1, only the septal point was used and in Study 2, the best results were achieved when only tracking the septal point. Pai et al. reported an excellent correlation ( $r = 0.93$ ) with septal measurements of the MAE from 4 chamber 2D images compared to radionuclide ejection fractions (LVEF-MUGA) (84). However, a single point measurement makes the solution less robust for regional pathology as e.g. myocardial scars. Carlhall et al. showed that the total MAE overestimates the amplitude and recommended a novel method of obtaining the MAE by identifying the true systole between mitral- and aortic valve closure (85). Without ECG or phonocardiogram, this method was not obtainable using the pocket-size device and our values may represent an overestimation of the true systolic values. However, the total MAE is an easy measurement to obtain, even in patients with reduced image quality (65). MAE is also highly reproducible (83). Alternatives could have been ‘eyeball’ assessment of the LVEF, LV dimensions and volumes. We could also have included a more complete cardiovascular assessment including valvular function, RV function and LA size. This would, however, require a higher competence level and longer education period, in particular among GPs who have very limited possibilities to discuss their findings.

A normal MAE does not rule out the possibility of the patient having cardiac dyspnoea. Measurement of MAE with a pocket-size device is not a substitute to a full echocardiographic examination by an expert; it is a supplement to the physical examination. Further work should focus on the added value of a pocket-size device as a supportive tool in decision making in primary care. To evaluate whether pocket-size ultrasound is useful in primary care, it should be assessed in patients suspected of having heart failure, and in addition to history taking, physical examination, and possibly also in addition to more readily available diagnostic tests such as natriuretic peptide measurements and electrocardiography

(86). However, the use of natriuretic peptides is limited by the availability and do not provide an answer during the consultation in the GPs office. Further studies should also assess whether the use of ultrasound in patients with dyspnoea improves diagnostics of heart failure and reduces the number of emergency admissions.

The first and second cardiologists were blinded to the GPs' measurement of MAE with pocket-size, but the first cardiologist was not blinded to his own M-mode measurements with the laptop scanner. This could have influenced the agreement (95% limits of agreement  $0.11 \pm 1.98$  mm). However, the most important comparison in Study 1 was measurements of MAE performed by GPs vs. a cardiologist with pocket-size ultrasound.

In Study 1, only seven GPs participated and 1 GP included more than half of the patients. The external generalisability would have been higher if more GPs were included in the study.

We tested our automatic algorithm for MAE measurement in a feasibility study limited by only 30 pocket-size recordings; this gives us a broad CI. These recordings were all expert-recordings which represent a second limitation, the target group for this kind of application will mainly be non-expert users which may be associated with reduced image quality. The accuracy of the algorithm should be suitable for successfully separating poor ventricles from normal ones and is comparable to previously reported numbers comparing M-mode and semi-automatic regular frame rate speckle-tracking (81). The MAE values are averagely underestimated, mainly resulting in false positive findings.

In Studies 3 and 4, the patients are examined in the in-hospital emergency setting, in Study 4 by internists experienced in both cardiovascular and abdominal ultrasound. All three internists were also board-certified cardiologists. The more realistic setting will be that chosen in Study 3, where the examinations were performed in the emergency room by a resident with a limited education in diagnostic ultrasound. The EACVI (former EAE) statements highlight

the importance of these physicians going through a dedicated training program with the emphasis on cardiac physiology and pathology (16).

The studies may be limited by a different organisation of the emergency room and the degree of specialised imaging procedures performed before the patient is admitted to the department compared to large centres in Europe or USA. Many non-university hospitals in Europe, as well as at other continents, have general medical departments. In addition, internists play a central role in most hospitals, being the coordinator of interdisciplinary diagnostic and therapeutic care. Finally, even in highly specialised units, the patients are increasingly multi-morbid (87). In our opinion, examination by pocket-size ultrasound devices is generalisable to other hospitals and countries as well, whether it is performed in the emergency department or the medical department.

In Study 4, an aortic dissection was diagnosed by pocket-size (Figure 4). It is important to emphasise that in such cases pocket-size may offer a fast-track to the correct diagnosis, but negative findings must not rule out further diagnostics if the clinician still suspects specific conditions.

Negative findings by abdominal ultrasonography were not systematically verified with other imaging modalities, but as shown, most cardiac and abdominal structures were assessed with high accuracy.

In Study 4, the diagnostic impact was the main issue. All of the clinicians who performed the ultrasound examinations had access to clinical information, including the preliminary diagnosis. However, the radiologist and cardiologist who performed the high-end reference imaging procedures were blinded to the result of the pocket-size ultrasound examination. The "end-point committee" was blinded as much as possible and the three members made separate decisions based on journal files and diagnostic tests blinded to the decisions of the other members. Among the 36 patients with a change in preliminary

diagnosis, the committee completely agreed in 33 (92%) patients and one member of the committee disagreed in the last 3 cases. In the latter cases, the minority of the committee voted for “diagnosis verified” and the majority voted for “diagnosis changed”. None of those who had the diagnosis changed following pocket-size ultrasound had this diagnosis changed thereafter. No patient underwent high-end echocardiography or MRI prior to inclusion and only 5 were examined with CT scans or abdominal ultrasound at the radiologic department prior to inclusion.

In spite of this, we suggest that implementing strategies and systems for routinely adding a pocket-size ultrasound examination to patients in medical departments are appropriate, but further studies must demonstrate the degree of education and training needed for the medical professionals performing these examinations.

## **8 Future perspectives**

Until now, several studies have shown good agreement on image quality between pocket-size examinations and examinations performed on high-end systems, which is perfect when performed by experts, and somewhat less when performed by non-experts.

However, the pocket-size devices still lag behind in functionality. The lack of modalities as pulsed and continuous Doppler makes them insufficient in some clinical scenarios. These are mainly scenarios where accurate quantification of valvular stenosis or regurgitation is warranted or hemodynamic assessment is a major part of the examination. Apart from the identification of an enlarged left atrium, there is no way to assess left ventricular filling pressures with pocket-size devices in patients with diastolic heart failure. In the intensive care units it not possible to calculate cardiac output with pocket-size devices.

Until today, the devices have been primarily intended for echocardiography, as they were only equipped with a cardiac sector probe. Recently a Smartphone-based imaging

system was released by MobiSante. This allows for a USB based connection of various probes. This may increase the different scenarios; linear probe for vascular assessment and ultrasound-guided vascular access as one example.

New clinical scenarios and less experienced users are both challenges for pocket-size ultrasound, and automation may allow for better quantification and reduced subjectivity (88). In this thesis, we present an automatic measurement of the MAE, with automated septum thickness measurement as another example (76). Automation may be an important part of the future imaging devices.

The miniaturisation process has made these scanners really pocket-sized. Physicians therefore have a new personal examination tool. Medical students must be taught the advantages of ultrasound and learn to understand the possibilities of organ or symptom-guided ultrasound as part of the physical examination. This will improve the diagnostic skills and the patients will take advantage of an earlier and correct diagnosis, leading to better overall treatment results.

## **9 Conclusions**

Pocket-size ultrasound is a new tool in our clinical daily life. The scanners are small, cheap and easy to handle. In this thesis we have shown that non-expert, as well as expert users in different clinical scenarios are able to use these devices correctly and increase their diagnostic precision.

When experts added a pocket-size ultrasound examination to the usual care diagnostics in the emergency room, they made important diagnostic changes in 1 of 5 patients admitted to a medical department, resulting in a completely different treatment strategy without time delay. Medical residents were after a targeted education in ultrasound able to obtain reliable

information of important cardiac structures and great vessels in patients admitted to a medical department.

In primary care, GPs were able to evaluate LV systolic function with pocket-size ultrasound using MAE as a surrogate marker. In order to aid inexperienced users, we have presented a fully automatic algorithm for measuring MAE. The algorithm is able to be run real-time on a pocket-size scanner. The accuracy of the algorithm makes it suitable for separating poor ventricles from normal ones. Further studies should be conducted to determine whether the use of this algorithm in dyspnoeic patients improves diagnostics of heart failure.

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# Paper I



## Assessment of left ventricular function by GPs using pocket-sized ultrasound

Ole Christian Mjølstad<sup>a,b,\*</sup>, Sten Roar Snare<sup>a</sup>, Lasse Folkvord<sup>c</sup>, Frode Helland<sup>d</sup>, Anders Grimsmo<sup>e</sup>, Hans Torp<sup>a</sup>, Olav Haraldseth<sup>a,f</sup> and Bjørn Olav Haugen<sup>a,b</sup>

<sup>a</sup>MI Laboratory, Department of Circulation and Medical Imaging, Norwegian University of Science and Technology, 7491 Trondheim, <sup>b</sup>Department of Cardiology, St. Olav's, Trondheim University Hospital, 7006 Trondheim, <sup>c</sup>Vikhammer Primary Care Centre, 7560 Vikhammer, <sup>d</sup>Hallset Primary Care Centre, 7027 Trondheim, <sup>e</sup>Department of Public Health and General Practice, Norwegian University of Science and Technology, 7491 Trondheim and <sup>f</sup>Department of Radiology, St. Olav's, Trondheim University Hospital, 7006 Trondheim, Norway.

\*Correspondence to Ole Christian Mjølstad, Akutten Hjerter-Lungesenteret, Prinsesse Kristinas gate 3, 7006 Trondheim, Norway; E-mail: ole.c.mjolstad@ntnu.no

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**Background.** Assessment of left ventricular (LV) function with echocardiography is mandatory in patients with suspected heart failure (HF).

**Objectives.** To investigate if GPs were able to evaluate the LV function in patients at risk of developing or with established HF by using pocket-sized ultrasound (pUS).

**Methods.** Feasibility study in general practice, seven GPs in three different Norwegian primary care centres participated. Ninety-two patients with reduced or at risk of developing reduced LV function were examined by their own GP using pUS. The scan (<5 minute) was done as part of a routine appointment. A cardiologist examined the patients <30 minutes afterwards with both a laptop scanner and pUS. Measurements of the septal mitral annular excursion (sMAE) were compared.

**Results.** In 87% of the patients, the GPs were able to obtain a standard view and measure the sMAE. There was a non-significant mean difference in sMAE between GP pUS and cardiologist laptop scanner of  $-0.15$  mm 95% confidence interval ( $-0.60$  to  $0.30$ ) mm. A comparison of the pUS recordings and measurements of sMAE made by GP versus cardiologist revealed a non-significant mean difference with acceptable 95% limits of agreement ( $-0.26 \pm 3.02$  mm).

**Conclusions.** With tailored training, GPs were able to assess LV function with sMAE and pUS. pUS, as a supplement to the physical examination, may become an important tool in general practice.

**Keywords.** Echocardiography, general practice, heart failure, left ventricular dysfunction, ultrasound.

### Introduction

Heart failure (HF) is a common disease in the community setting.<sup>1</sup> At the same time, the sensitivity of clinical signs is low and GPs have a limited toolbox available to provide a rapid diagnosis.<sup>2</sup> Assessment of left ventricular (LV) function with echocardiography is mandatory in patients with suspected HF.<sup>3</sup> However, most echocardiographic scanners are located in hospitals and operated by a limited number of highly trained personnel. In the study group on

HF Awareness and Perception in Europe survey, only 50% of primary care physicians could obtain echocardiograms directly (16%) or via specialists (34%) within 1 month.<sup>4</sup>

HF is prevalent and according to the European Society of Cardiology, there are 15 million patients with HF among their member countries that comprise a population >900 million.<sup>3</sup> HF accounts for 2% of national expenditure on health due to hospital admissions.<sup>5</sup> To prevent emergency admissions and readmissions is thus a goal for the health authorities.

The development of pocket-sized, easy-to-use and affordable ultrasound machines might help spread the use of echocardiography to general practice. The accuracy of these scanners has been proven in the hands of experts.<sup>6</sup> However, the ability of GPs to use these machines is not known. The recently published statement from the European Association of Echocardiography on the use of pocket-sized imaging devices emphasizes that handheld ultrasound represents a tool for fast initial cardiac assessment as a complement to the physical examination and that it may work in triaging of the patient in need of a complete echocardiographic examination.<sup>7</sup>

The standard way to assess LV systolic function is to measure the ejection fraction (LV-EF) with the Simpson's technique.<sup>8</sup> However, this method requires good image quality for adequate tracing of the endocardial borders. The mitral annular excursion (MAE) is an easily obtainable surrogate measure of LV systolic function.<sup>9</sup> Several studies have shown a high correlation between the MAE and LV-EF determined by biplane area-length method.<sup>10–12</sup> An excursion >10 mm represents a normal LV-EF defined as EF 50%–55%.<sup>10,13</sup> A reduction of MAE precedes that in circumferential systolic function in hypertensive cardiomyopathy and correlates with severity of valve disease in aortic stenosis.<sup>9</sup> The MAE has been shown to be an independent prognostic variable for survival and has a negative correlation with brain natriuretic peptide (BNP).<sup>14,15</sup>

The aim of this study was to investigate if GPs, after an 8 hour training course, were able to do a focussed assessment of the LV function by measuring the septal mitral annular excursion (sMAE) in patients at risk of developing or with established HF, using pocket-sized ultrasound (pUS).

## Methods

The study was performed in three different primary care centres in Norway. Altogether, seven GPs participated in the study.

### Subjects

The study population (Table 1) comprised 92 patients, 61 (66%) males, median (range) age was 72.5 (38–88) years. Patients with at least one of the following characteristics—systolic HF (32%), earlier myocardial

infarction (63%) or arterial hypertension (40%) were recruited to the study by their GPs. The GPs searched their archives for patients with a relevant International Classification of Primary Care diagnosis: K75 myocardial infarction, K77 HF and K87 hypertension complicated. Some of the patients had a previous echocardiographic examination, in such case, the GP was specifically told not to checkup these results. There were no specific exclusion criteria and no selection according to echogenicity. The three different centres included 19, 21 and 52 patients. The different GPs included between 3 and 52 patients. Written informed consent was obtained from all participants.

### Ultrasound imaging examination

None of the participating doctors had any experience with performing echocardiography, although all of them had observed demonstrations of echocardiographic examinations. All GPs covered the entire field of general practice.

The participating GPs received a total of 8 hours of supervised training. The lecturer throughout this course was a cardiologist certified in echocardiography in accordance with the requirements specified by the Norwegian Medical Association. In the first 4 hours of the course, the GPs were taught the very basic principles of theoretical echocardiography and anatomy of the heart as visualized by ultrasound. The GPs were taught how to examine the patients positioned in the left lateral decubitus position and how to make an optimal apical four-chamber view. They were also taught how to analyse the LV function by measuring the sMAE. The next 4 hours consisted of practical training, including practicing on each other and on 3–5 patients. After the supervised training period, they had the possibility to practice with the scanner on their own for a week before the study started.

All patients were examined in the GPs' primary care centres. Images were obtained by the seven GPs using a pUS scanner capable of B-mode and colour flow imaging (Vscan; GE Healthcare, Horten, Norway). An algorithm enables automatic storage and looping of a cardiac cycle without electrocardiogram signal. An examination contained a recording of an apical four-chamber view. This added no more than 5 minutes to the consultation.

In an adjacent examination room, a full reference examination was made by a cardiologist certified in echocardiography using a laptop scanner (Vivid I; GE Healthcare). This examination was performed immediately (<30 minutes) after the GP finished his/her examination and according to a complete protocol for a transthoracic echocardiogram including two-dimensional imaging, Doppler and tissue Doppler recordings. Immediately after having performed the complete scan, the cardiologist also examined all the patients with the pUS scanner.

TABLE 1 Basic characteristics of 92 study participants

	N (%) <sup>a</sup>
Age, years median (range)	72.5 (38–88)
Male	61 (66%)
HF	29 (32%)
Previous myocardial infarction	58 (63%)
Hypertension	37 (40%)

<sup>a</sup>Data are N (%) unless specified.

### Data analyses

The pUS recordings were exported to the commercially available software Vscan Gateway (GE Healthcare) on a standard laptop PC. The GP did the analysis of the sMAE in the loop of one cardiac cycle. The measurement was made by scrolling the two-dimensional loop from end diastole to end systole and then measuring the total displacement of the septal part of the mitral annulus, which represents the total displacement throughout a cardiac cycle (Fig. 1). The Vscan has a limited field of view of up to 75° for black and white imaging. Due to dropouts and out-of-plane movement of the lateral part of the mitral ring, the septal part was chosen for all measurements. The recordings were analysed by the GP that actually examined the patient. All the recordings acquired by the GPs were also analysed offline by a second cardiologist certified and experienced in echocardiography.

The reference examinations performed on the laptop scanner were exported to the commercially available Echo PAC PC version BT 09 (GE Healthcare, Horten, Norway). In this full reference examination, the M-mode recording of the mitral annulus was measured according to the method performed in previous studies (Fig. 2).<sup>11,12</sup> Only septal measurements were used in the comparisons with the pUS recordings.

### Statistics

The null hypothesis corresponded to no difference between the sMAE measured by the GPs and a cardiologist. Including 92 patients resulted in power >90% at the 5% significance level for detecting a difference in 2 mm in sMAE, assuming one SD of 1.51 mm.

Continuous values are expressed as median and range. Because the differences were normal distributed, we used paired *t*-test to compare sMAE measured by the GPs and the cardiologist. When comparing the two different scanners, the laptop scanner is considered the gold standard and the results are reported as mean difference and 95% confidence interval (CI). Bland and Altman analysis was used to assess agreement between different operators and measurements of sMAE with pUS.<sup>16</sup> The coefficient of repeatability and mean error of the sMAE were calculated for pocket-sized data. The inter-observer coefficient of repeatability was defined as 1.96 SD of the differences in repeated measurements. The mean error was defined as the absolute difference in between two sets of observations divided by the mean of the observations  $\pm$  SD%. Statistical analyses were performed using SPSS PASW Statistics 18.0.

## Results

Table 1 shows the basic characteristics of the patients. In 80 (87%) of patients, the GPs were able to obtain

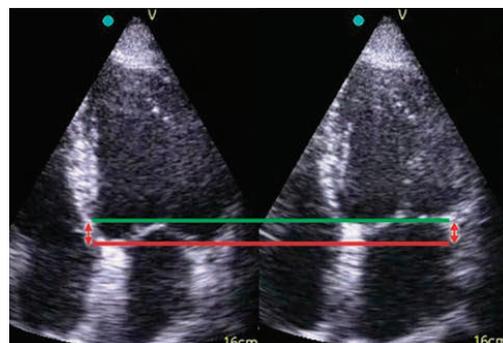


FIGURE 1 Two-dimensional recording of the left ventricle in end diastole (left) and end systole (right). The red line indicates the position of the mitral annular septum in end diastole and the green line, the position in end systole. The distance between the lines (red arrows) represents the total distance/excursion by the septal part of the mitral annulus through a complete heart cycle

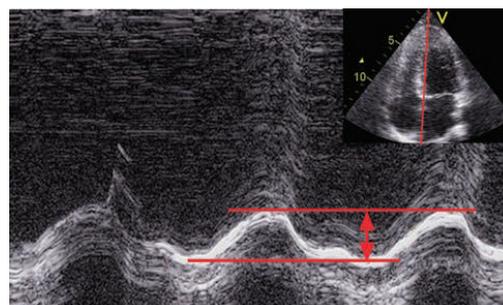


FIGURE 2 M-mode registration of sMAE. The distance between the red lines (arrow) indicates the total distance/excursion by the septal part of the mitral annulus through a complete heart cycle

a four-chamber view of such a quality that they were able to measure the sMAE. Seven of the remaining recordings were of such a bad quality that further analysis was impossible and in five of the recordings, an image was recorded instead of a loop. The pUS examination was performed without delaying the standard consultation. A full reference examination and a pocket-sized recording were obtained in all 92 patients by the cardiologist. The LV-EF ranged from 25% to 70% with a median of 52%. The sMAE ranged from 4.0 to 15.0 mm with a median of 10.0 mm.

There was a non-significant mean difference in sMAE between GP pUS and cardiologist laptop scanner of  $-0.15$  mm 95% CI  $(-0.60$  to  $0.30)$  mm. Comparing the two different scanners, when both were operated by the first cardiologist, there was a non-significant mean difference in sMAE of  $0.11$  mm 95% CI  $(-0.10$  to  $0.32)$  mm.

Comparing the measurement of the sMAE made by the GPs and the sMAE made by the cardiologist both using pUS, the 95% limit of agreement was  $-0.26 \pm 3.02$

mm and there was virtually no bias or trend in the data (Fig. 3). When a second cardiologist did the off-line analysis on the recordings acquired by the GPs,

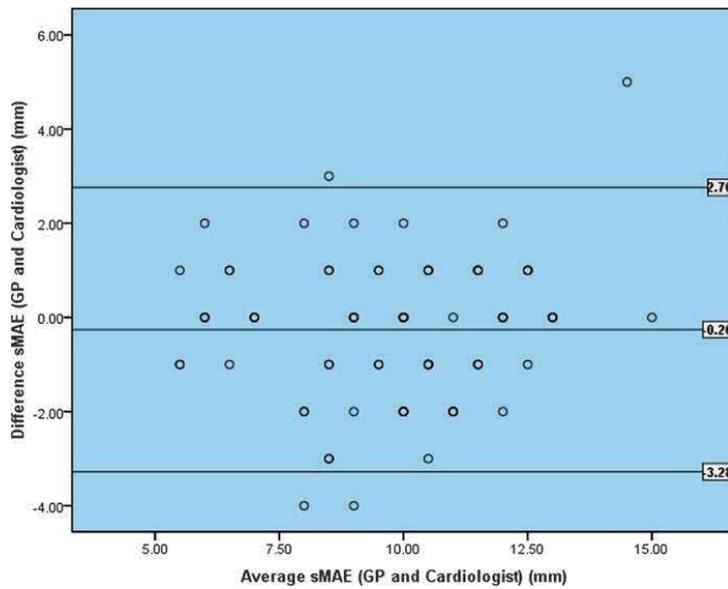


FIGURE 3 Ninety-five per cent limits of agreement between measurements of sMAE with pUS (Vscan) performed and analysed by the GPs versus the cardiologist

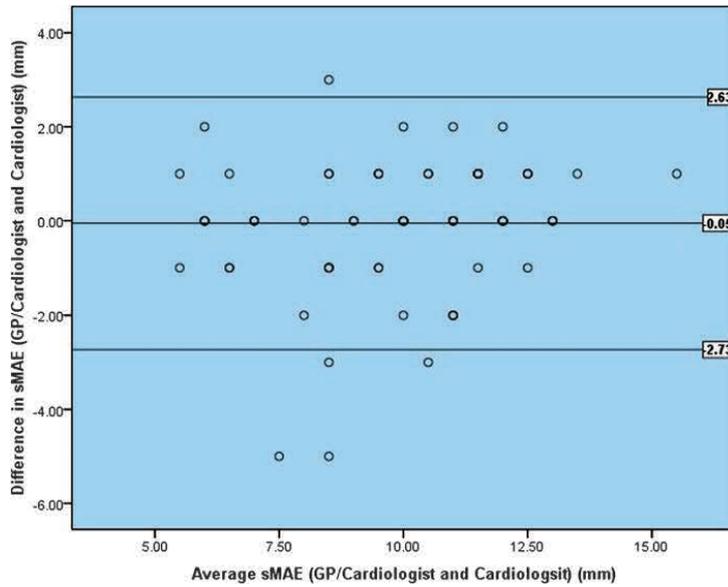


FIGURE 4 Ninety-five per cent limits of agreement between measurements of sMAE with pUS (Vscan) performed by the GPs and analysed by the second cardiologist versus the cardiologist

the 95% limit of agreement narrowed to  $-0.05 \pm 2.68$  mm (Fig. 4). There were no significant differences in measurements of sMAE, neither between the different operators or the different scanners. The measurements for each of the three centres are presented in Table 2. The study was not designed or powered to perform statistical analysis for each centre and data are presented as mean difference  $\pm$  SD.

Sensitivity and specificity of GP operated pUS to detect a reduced LV function defined as an sMAE  $<10$  mm measured by the cardiologist with a laptop scanner was 83.3% 95% CI (66.4–92.7) and 77.6% 95% CI (64.1–87.0) respectively. The negative and positive predictive value were 88.4% and 69.4%, respectively. When the offline analysis of GP recordings was performed by the second cardiologist, sensitivity and specificity increased to 77.4% 95% CI (60.2–88.6) and 85.4% 95% CI (72.8–92.8) and the negative and positive predictive value 85.4% and 77.4%, respectively.

The inter-observer coefficient of repeatability for pocket-sized recordings and measurement of sMAE was 3.1 mm and the mean error was  $12.2\% \pm 11.5\%$ .

## Discussion

In this study, we have shown that it is possible for GPs, after a limited period of focussed training, to use a pUS scanner to assess a surrogate marker for global LV function in 87% of the patients with or at risk of developing reduced LV function. The pUS examination could easily be performed in 5 minutes during a routine consultation in the GPs office. The sMAE was selected as a robust parameter and easily obtainable measurement of the LV function. There was no significant difference between measurements of sMAE obtained by the GPs and a cardiologist, neither with a laptop scanner and the gold standard M-mode nor with pUS with its limited frame rate. When operated by the cardiologist, pUS offered the same accuracy as a laptop scanner when evaluating the sMAE.

GPs have limited tools available for rapid assessment of patients with dyspnoea and there is a lack of access to echocardiography.<sup>1,2,17</sup> To our knowledge, our study is the first that has assessed whether a number of GPs, in different primary care centres, can do an examination with pUS to assess LV function in patients at risk of developing or with established HF. The training of GPs in our study was limited but specifically tailored to the information they should obtain from this new class of devices. This strategy is fully supported by the recent guidelines issued from the European Association of Echocardiography regarding the use of these new machines in that users should focus their examination to answer a specific question and use this as a tool to support their physical examination.<sup>7</sup> The scan was integrated in the physical examination and was performed in  $<5$  minutes. The sensitivity and negative predictive values were high.

In agreement with our study, previous studies have shown that echocardiography may provide information even in the hands of inexperienced users. Decara *et al.*<sup>18</sup> showed how hand-carried ultrasound devices used by medical students significantly resulted in a more accurate bedside diagnosis. Lucas *et al.*<sup>19</sup> showed that the diagnostic accuracy of hand-carried ultrasound devices performed by hospitalists after a brief training programme was moderate to excellent for six important cardiac abnormalities. Lipczynska *et al.*<sup>20</sup> found that hand-carried ultrasound examinations of the heart performed by an internist with 4 weeks of training can provide important prognostic information, independent of BNP. Similar to the duration of training in our study, Vignon *et al.*<sup>21</sup> found that intensive care resident doctors were able to rule out LV dysfunction (LV-EF  $< 50\%$ ) by eyeballing after an 8 hours focussed training programme.

According to the current guidelines, the recommended method for evaluating LV function is the EF calculated from the biplane method of discs (modified Simpsons' rule).<sup>8</sup> This is not an easy method for an inexperienced users mainly because endocardial

TABLE 2 The mean difference for the different comparisons for the total study population and for each of the three centres

	Total (n = 92)	Centre 1 (n = 21)	Centre 2 (n = 52)	Centre 3 (n = 19)
pUS GP versus laptop <sup>a</sup>	-0.15 mm (-0.60 to 0.30)	0.77 mm ( $\pm 1.56$ )	-0.73 mm ( $\pm 1.96$ )	1.18 mm ( $\pm 2.09$ )
pUS GP/cardiologist versus laptop <sup>a</sup>	0.08 mm (-0.29 to 0.44)	0.65 mm ( $\pm 1.32$ )	-0.24 mm ( $\pm 1.68$ )	0.64 mm ( $\pm 1.43$ )
pUS cardiologist versus laptop <sup>a</sup>	0.11 mm (-0.10 to 0.32)	0.57 mm ( $\pm 1.29$ )	-0.09 mm ( $\pm 0.93$ )	0.19 mm ( $\pm 0.66$ )
pUS GP versus pUS cardiologist <sup>b</sup>	-0.26 mm ( $\pm 3.02$ )	0.12 mm ( $\pm 1.41$ )	-0.65 mm ( $\pm 1.37$ )	1.0 mm ( $\pm 1.79$ )
pUS GP/cardiologist versus pUS cardiologist <sup>b</sup>	-0.05 mm ( $\pm 2.68$ )	0.00 mm ( $\pm 1.50$ )	-0.18 mm ( $\pm 1.38$ )	0.45 mm ( $\pm 1.04$ )

In comparisons between the different scanners, the laptop scanner is considered the gold standard and the 95% CI of the mean difference is given for the total population and mean difference  $\pm$  SD for each of the centres. In comparisons between different operators both using pUS, the 95% limit of agreement is given for the total population and mean difference  $\pm$  SD for each of the centres. pUS GP, pUS performed and analysed by the GP; pUS cardiologist, pUS performed and analysed by the cardiologist; pUS GP/cardiologist, pUS performed by the GP and analysed by the second cardiologist; laptop, echocardiography performed and analysed by the cardiologist using a laptop scanner.

<sup>a</sup>Data are mean difference and 95% CI for the total population and mean difference  $\pm$  SD for each centre.

<sup>b</sup>Data are mean difference and 95% limits of agreement for the total population and mean difference  $\pm$  SD for each centre.

definition requires a high image quality. Tracing of endocardial borders in both end diastole and end systole in two imaging planes are required to calculate the LV-EF in this method [EF =  $100 \times (\text{end-diastolic volume} - \text{end-systolic volume}) / \text{end-diastolic volume}$ ]. Analysing the MAE is another established method for evaluating LV function.<sup>10-12</sup> This is a simple method, it is highly reproducible and it is feasible even in patients with poor image quality.<sup>10,22</sup> No studies have been found to report inter-observer variability for measurement of MAE using pocket-sized scanners, only high-end scanners operated by experts. In one study, Thorstensen *et al.*<sup>22</sup> averaged M-mode excursion measurements in four points (septal, lateral, inferior and anterior wall) and reported 4% mean error and a coefficient of repeatability of 1.6 mm. Yuda *et al.*<sup>10</sup> reported 6.4% mean error, also using M-mode measurements. Using a speckle tracking approach, Tsang *et al.*<sup>23</sup> reported mean errors of 12.2% in apical four-chamber images and 12.7% in two-chamber images. In our study, calculating the mean error and coefficient of repeatability between the GP and the first cardiologist yields 12.1% and 3.08 mm.

The GPs had a limited amount of training and did only septal measurements of the MAE from four-chamber two-dimensional images as opposed to others that used the average of four measure points with M-mode along the mitral ring from the four and two chamber view.<sup>11,12</sup> However, Pai *et al.*<sup>24</sup> reported an excellent correlation ( $r = 0.93$ ) with septal measurements of the MAE from four-chamber two-dimensional images compared to radionuclide EFs (Multi Gated Acquisition Scan).

One limitation in our study is that the number of GPs was only seven, a higher number of participating GPs would have increased the generalizability. A further limitation is that in 13% of the patients, the GP was not able to measure the sMAE, this was mainly related to technical problems and would probably be a minor problem with further training. The first and second cardiologist was blinded to the GPs measurement of sMAE with pUS, but the first cardiologist was not blinded to his own M-mode measurements with the laptop scanner. This could have influenced the agreement between the two different scanners.

A normal sMAE does not rule out the possibility of the patient having cardiac dyspnoea and is not a substitute for a full echocardiographic examination by a cardiologist. The MAE is a surrogate marker of LV function, predominantly systolic function but also diastolic, and should be evaluated in the context of other variables such as valvular function. Yet, an examination with pUS is available at the GP office any time off-day and may allow an earlier and more correct care, both when systolic dysfunction is shown and when this is ruled out.

Further work should focus on the added value of pUS as a supportive tool in decision making in

primary care and to determine whether the use of ultrasound in dyspnoeic patients improves diagnostics of HF and reduces the number of emergency admissions. Future work should also introduce software that may aid inexperienced users in getting better images and make automatic measurements of the MAE.<sup>25</sup> It is also important to formalize training programmes in order to avoid misuse.

## Conclusions

With tailored training, GPs in this study were able to assess LV function with sMAE and pUS. pUS, as a supplement to the physical examination, may become an important tool in general practice, but further studies are needed to see if this improves diagnostics of HF in general practice.

## Acknowledgements

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## Declaration

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Ethical approval: Regional Committee for Medical and Health Research Ethics (reference number: 4.2009.257) and the Norwegian Social Science Data Service (reference number: 21549/2/LT).

Conflict of interest: none.

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## Paper II





● *Original Contribution*

## FAST AUTOMATIC MEASUREMENT OF MITRAL ANNULUS EXCURSION USING A POCKET-SIZED ULTRASOUND SYSTEM

STEN ROAR SNARE,\* OLE CHRISTIAN MJØLSTAD,\*<sup>†</sup> FREDRIK ORDERUD,<sup>‡</sup> BJØRN OLAV HAUGEN,\*<sup>†</sup>  
and HANS TORP\*

\*Department of Circulation and Medical Imaging, Norwegian University of Science and Technology (NTNU), Trondheim;  
<sup>†</sup>Department of Cardiology, St. Olavs University Hospital, Trondheim; and <sup>‡</sup>GE Vingmed Ultrasound, Oslo, Norway

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**Abstract**—We present a fast, automatic method for mitral annulus excursion measurement using pocket-sized ultrasound (PSU). The motivation is to provide PSU users with a rapid measurement of cardiac systolic function. The algorithm combines low-frame-rate tolerance, computational efficiency and automation in a novel way. The method uses a speckle-tracking scheme, initialized and constrained by a deformable model. A feasibility study using 30 apical four-chamber PSU recordings from an unselected patient population revealed an error of (mean  $\pm$  SD)  $-1.80 \pm 1.96$  mm,  $p < 0.001$ , when compared with manual anatomic m-mode analysis using laptop scanner data. When only septal side excursion was measured, the mean error was  $-0.27 \pm 1.89$  mm,  $p < 0.001$ . The accuracy is comparable with previously reported results using semiautomatic methods and full-size scanners. The computation time of 3.7 ms/frame on a laptop computer suggests that a real-time implementation on a PSU device is feasible. (E-mail: sten.r.snare@ntnu.no) © 2011 World Federation for Ultrasound in Medicine & Biology.

**Key Words:** Pocket ultrasound, Hand-carried ultrasound, Feature tracking, Block matching, Echocardiography.

### INTRODUCTION

The development of hand-carried ultrasound (HCU) has branched in two directions (Spencer 2008). Whereas one direction aims to close the performance gap between HCU and full-size scanners, the other direction heads toward miniaturization. Recently, several commercial equipment manufacturers have launched pocket-sized ultrasound (PSU) devices capable of echocardiography, such as Siemens/Acuson P10 and GE Healthcare Vscan. The advent of truly pocket-sized equipment opens up for new applications of ultrasound.

Cardiac examination is one of the clinically interesting applications for portable ultrasound, and this topic has already been investigated in several studies (Atherton 2010; Culp et al. 2010; Vourvouri et al. 2003; Egan and Ionescu 2008; Spencer 2008; Spevack et al. 2003). Atherton (2010) stated that HCU is promising as a screening tool for asymptomatic subjects, but that the specificity is high only for experienced sonographers. We believe that because of their smaller size and lower

cost, PSU units will more often be operated by inexperienced users and would benefit from having applications actively *aiding* these users in detecting heart disease. One way of doing this could be to include **automatic** or **semiautomatic** cardiac measurements.

Ejection fraction (EF) is the most commonly used measurement for global systolic left ventricular function. Correct measurement of EF using 2-D ultrasound is difficult and requires good visibility of all segments of the left ventricle (LV). The mitral annulus excursion (MAE) measurement requires good image quality only in the base and has shown to correlate with EF (DeCara et al. 2005; Tsang et al. 2010; Emilsson et al. 2000; Elnoamany and Abdelhameed 2006).

Several recent papers (Nevo et al. 2007; Eto et al. 2005; DeCara et al. 2005; Tsang et al. 2010) address the topic of semiautomatic measurement of MAE. Pocket-sized scanners typically have a much lower frame rate than regular scanners, which is a challenge for speckle-tracking approaches. One paper has addressed low-frame-rate tracking (Nevo et al. 2007) but no published algorithm has been shown to combine computational efficiency with low-frame-rate tolerance. We propose a novel, highly efficient method for measurement of MAE on low-frame-rate (20 Hz) ultrasound data from

Address correspondence to: Sten Roar Snare, Department of Circulation and Medical Imaging, Norwegian University of Science and Technology, PO Box 8905, Med Tech Research Centre, 7491 Trondheim, Norway. E-mail: sten.r.snare@ntnu.no

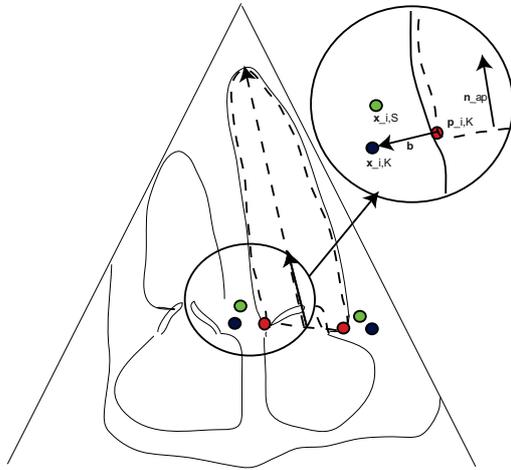


Fig. 1. The Kalman model mitral annulus (MA) points,  $\mathbf{p}_{i,K}$  and the corresponding Kalman tracking points  $\mathbf{x}_{i,K}$ .  $\mathbf{x}_{i,S}$  denote the final speckle tracking points. Also note the vector from the atrioventricular plane to the cardiac apex,  $\mathbf{n}_{ap}$  and the vector  $\mathbf{b}$  from the model MA point to the model-based tracking point.

a pocket-sized scanner, combining speckle tracking and model-based segmentation of the left ventricle. The system is designed to be fully automatic and capable of

real-time operation on pocket-sized ultrasound scanners. Here we will present the method and provide results from a feasibility study.

## MATERIALS AND METHOD

The algorithm has two main parts. The first part is the Kalman filter segmentation, which uses a Kalman filter to fit a deformable model of the LV to the image data. The second part is a speckle tracker, which is a variant of the commonly used sum of absolute differences (SAD) speckle tracker, using correlation-weighted spatial averaging. The Kalman filter segmentation is used to initialize the speckle tracker and prevent tracking drift. We used a weighted averaging scheme, combining the SAD fit and the movement of the deformable model, to derive the new kernel points for the speckle tracker. The system either loads Cartesian data directly or beamspace data from dicom files. In the latter case, an in-house scan conversion is used to generate Cartesian image data.

### Kalman filter segmentation

The Kalman filter segmentation is founded on the work by Orderud and Rabben (2008) and Orderud et al. (2008). We have used nonuniform rational B-splines (NURBS) to create the deformable model. NURBS were chosen because of their flexibility and versatility.

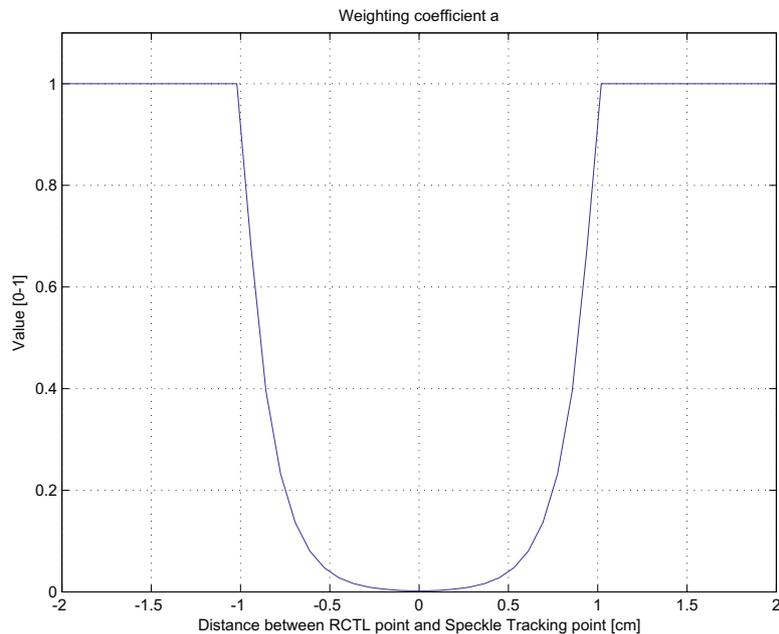


Fig. 2. Weighting function for combining speckle tracking and Kalman filter results. As long as the difference between the Kalman-based tracking point  $\mathbf{x}_{i,K}$  and the speckle tracking point  $\mathbf{x}_{i,S}$  is  $<5$  mm, the position of the next tracking kernel is mainly based on the speckle tracking. If the difference is  $>1$  cm, the parametric model is used to position the new kernel.

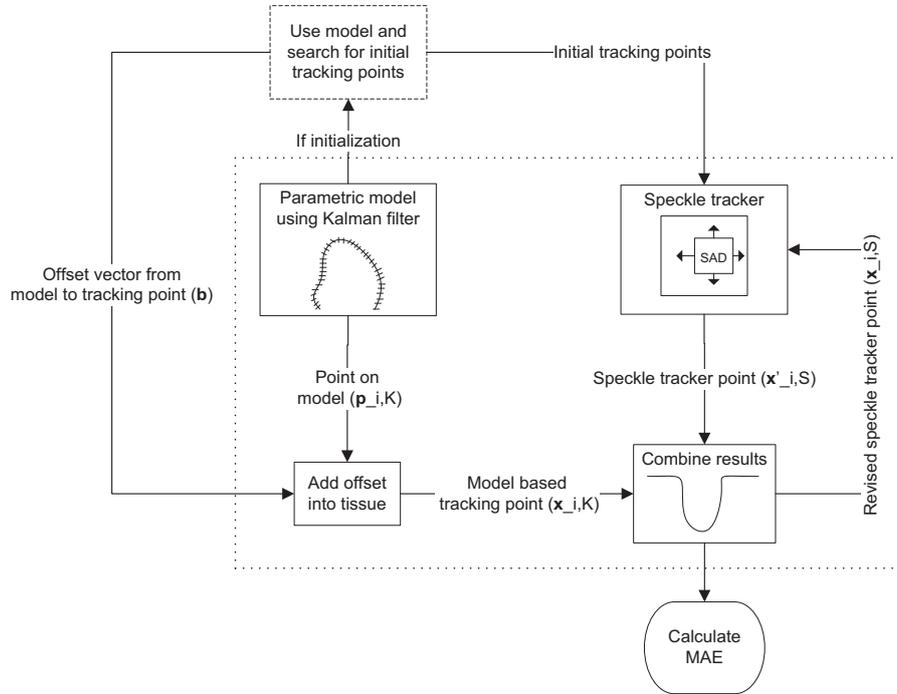


Fig. 3. Flowchart illustrating the main components of the MAE measurement system. A parametric model is fitted to the image data using a Kalman filter. Upon initialization of the speckle tracker, the model is used to calculate initial tracking points and a vector,  $\mathbf{b}$ , pointing from the model to these initial tracking points. After initialization, the speckle tracker and Kalman filter is run in parallel. For each frame, the vector  $\mathbf{b}$  is used to calculate new tracking kernel points based on the movement of the deformable model,  $\mathbf{x}_{i,K}$ . These results are combined with the SAD fit from the speckle tracker,  $\mathbf{x}'_{i,S}$ , yielding the corrected tracking points  $\mathbf{x}_{i,S}$ . These points are used for calculation of MAE, as well as for new speckle tracker kernel points in the next frame.

Use of Kalman filter for 2-D segmentation using B-splines has been published by Blake *et al.* (1993), Blake (1995), Jacob *et al.* (1999), Jacob *et al.* (2001) and Jacob *et al.* (2002). As system states, the Kalman filter uses pose parameters and normal displacements of the NURBS control points. The motion model in the filter is simple, and the prediction is based on the previous step only. Edge detection measurements, as well as block matching, are used as measurement input to the Kalman filter. By assimilating the measurements into information space, an efficient implementation is possible. A detailed description of the Kalman filter segmentation scheme can be found in Appendix A.

The result of the Kalman filter segmentation is an efficient and robust model of the LV. By selecting model points in the basal region of the model, it is now possible to approximate MAE using the model only. Initial tests proved this approach to be inaccurate. Especially around end-diastole, the model was not able to accurately track the movement of the atrioventricular (AV) plane when

facing challenging image quality. Our solution has been to use the Kalman filter model as initialization and drift compensation for a regular speckle tracker. The purpose is to combine the accuracy of speckle tracking with the robustness and low-frame-rate tolerance of the Kalman filter.

#### Speckle tracking

AV plane speckle tracking should be done around the hinge point for the mitral valve leaflets. In practice, this region can be very blurred. When a clinician is selecting a point for speckle tracking, he should select a bright speckle in an anatomically correct position. It is challenging to automate this selection process. We have chosen to first locate an asymmetric region of interest (ROI) at the model corner points, and then do a search for the brightest pixel within that ROI. Because we are using data from both pocket-sized and laptop systems, two different setups are required. Values for the laptop system are put in parentheses. The ROI size is  $10 \times 11$

mm ( $5 \times 5$  mm) and centered 1 mm (1 mm) left and 3 mm (1.5 mm) down from the septal corner point, considering an apical four-chamber view. On the lateral side, the ROI is centered 4 mm (2 mm) to the right and 3 mm (3 mm) down from the corner point.

For simplicity, we will now only consider one point at a time. We denote the detected initial tracking point, lateral or septal, as  $\mathbf{x}_{0,S}$ . The subscript S means “Speckle.” We now search for the closest point on the deformable model and denote it as  $\mathbf{p}_{0,K}$ . The subscript K means “Kalman.” The vector from the point on the model to the tracking point is denoted as  $\mathbf{b}$ . Using the parametric coordinate of  $\mathbf{p}_{0,K}$  and the deformable model, we will always have knowledge about  $\mathbf{p}_{i,K}$ , where  $i$  means frame number

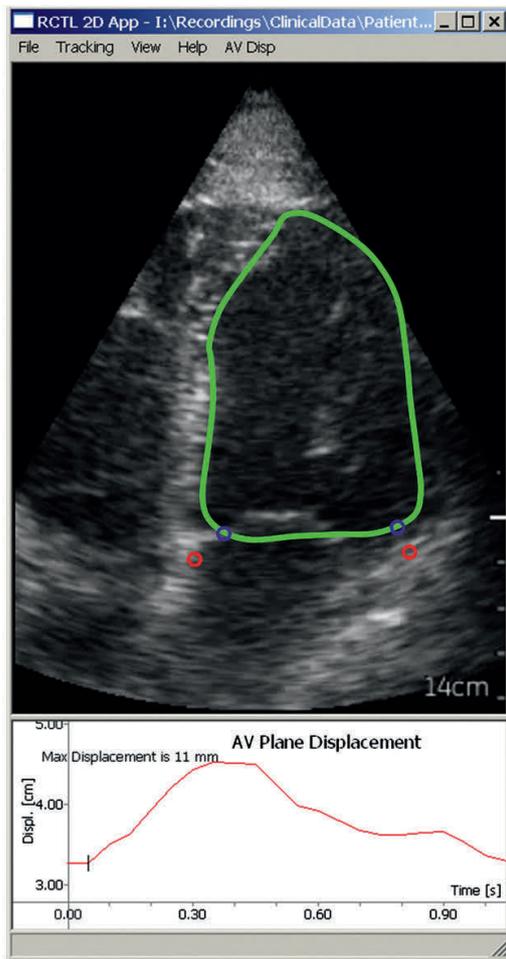


Fig. 4. Example segmentation from a PSU recording. The circles in the basal region of the model correspond to  $\mathbf{p}_{i,K}$  and the circles in the myocardium correspond to  $\mathbf{x}_{i,S}$ .

(Fig. 1). We find the corresponding Kalman filter–based tracking point for all frames:

$$\mathbf{x}_{i,K} = \mathbf{p}_{i,K} + \mathbf{b}. \quad (1)$$

In a  $3 \times 3$ -mm ( $4 \times 4$  mm) region around  $\mathbf{x}_{i,S}$ ,  $N_{avg} - 1$  surrounding points for averaging are selected. The  $N_{avg}$  points become the center points for the block-matching kernels in frame  $i$ . We have chosen to use 26 (36) points for averaging. Each kernel has a size of  $5 \times 6$  mm ( $5 \times 5$  mm). Search windows are  $7 \times 14$  mm ( $8 \times 9$  mm). A SAD fit of the kernels results in  $N_{avg}$  displacement vectors. These are combined using the weighted average of the  $N_{avg}$  displacement vectors. The weights are calculated from the Pearson's sample correlation coefficient between the kernel and the best fit for each of the averaging points. This means that tracking points where there is high correlation between the kernels in consecutive frames are the priority. Tracking points with a correlation coefficient below a threshold,  $T_c = 0.4$ , are discarded. The average displacement vector is denoted  $\bar{\mathbf{d}}_{d,i}$ . The new position of the tracking points  $\mathbf{x}'_{i,S}$  becomes

$$\mathbf{x}'_{i,S} = \mathbf{x}_{i-1,S} + \bar{\mathbf{d}}_{d,i}, \quad i = \{1, 2, \dots\}. \quad (2)$$

In regular speckle tracking, the standard solution would be to set  $\mathbf{x}_{i,S} = \mathbf{x}'_{i,S}$ , add points for averaging and repeat the process. This would be sensitive to drift and

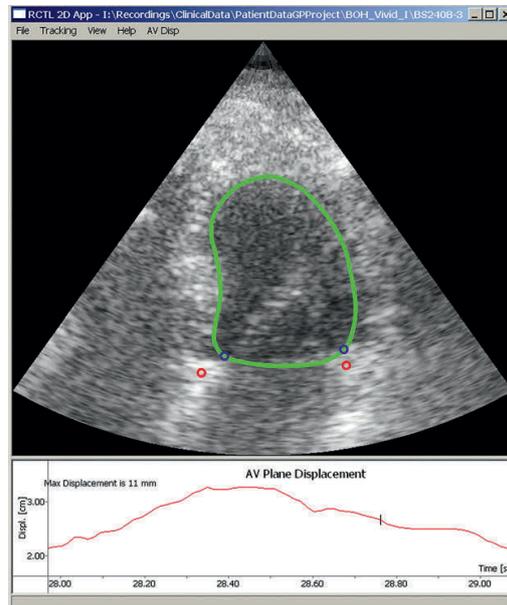


Fig. 5. Example segmentation from a HCU recording (same patient as in Fig. 4). The circles in the basal region of the model correspond to  $\mathbf{p}_{i,K}$  and the circles in the myocardium correspond to  $\mathbf{x}_{i,S}$ .

Table 1. Table summarizing the MAE measurement results using PSU and HCU data

Method	MAE (mm)	MAE (mm)	Paired <i>t</i> -test (mean $\pm$ SD) (mm)	Pearson's <i>r</i>	95% mean CI (mm)
PSU	5.5	2.2	$-1.80 \pm 1.96$ $p < 0.001$	0.62 $p < 0.001$	(-2.53, -1.07)
PSU (septal)	3.0	1.6	$-0.27 \pm 1.89$ ( $p = 0.446$ )	0.61 $p < 0.001$	(-0.97, 0.44)
HCU	5.5	2.1	$-1.17 \pm 2.32$ ( $p = 0.010$ )	0.61 $p < 0.01$	(-2.03, -0.30)
HCU (septal)	4.0	1.4	$-0.13 \pm 1.78$ ( $p = 0.684$ )	0.69 $p < 0.001$	(-0.80, 0.53)
PSU (semiautomatic)	4.5	2.0	$-1.57 \pm 1.72$ $p < 0.001$	0.69 $p < 0.001$	(-2.21, -0.92)
HCU (semiautomatic)	4.0	1.8	$-1.40 \pm 1.69$ $p < 0.001$	0.64 $p < 0.001$	(-2.04, -0.75)

Both fully automatic and semiautomatic results are presented. In case of automatic analysis, the results when only using septal measurements are also provided. The results are presented as maximum absolute error, mean absolute error, paired *t*-test results (mean  $\pm$  SD), Pearson's correlation coefficient and 95% mean confidence interval. All values, except the correlation coefficient, are measured in millimeters.

is likely to fail on low frame-rate loops. We thus combine this result with the model from the Kalman filter segmentation.

Three main criteria exist for this combination process:

- Speckle-tracking results should be given priority as long as  $\|\mathbf{x}_{i,K} - \mathbf{x}'_{i,S}\|$  is small or moderate.
- When  $\|\mathbf{x}_{i,K} - \mathbf{x}'_{i,S}\|$  is large, the Kalman filter-derived points should rapidly pull the speckle tracker toward the correct region.

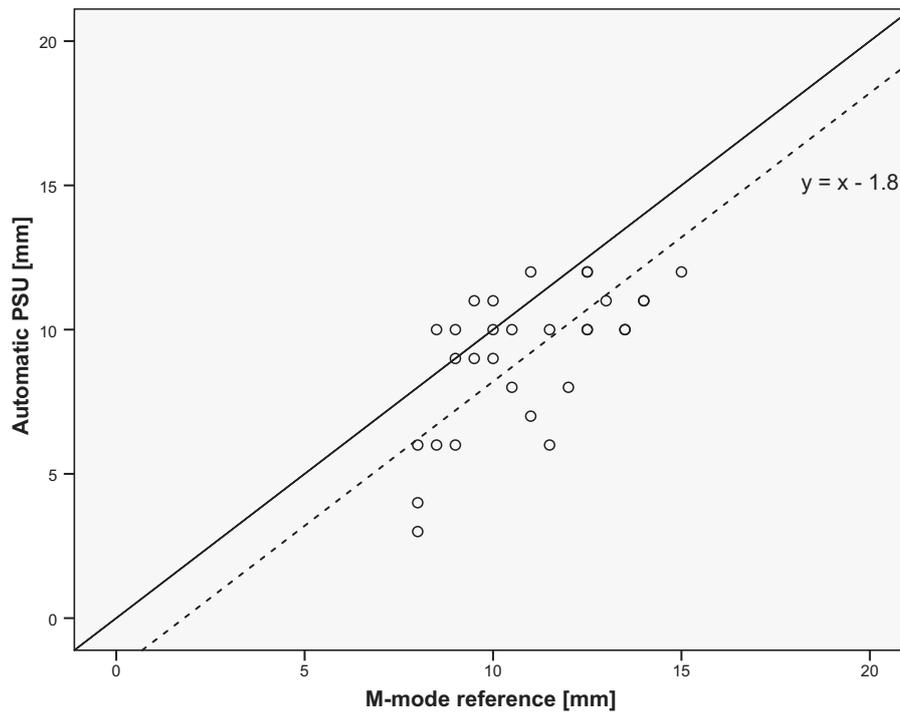


Fig. 6. Scatter plot with the PSU results along the vertical axis and the m-mode reference values along the horizontal axis. The solid line is the reference unity line ( $y = x$ ). The dashed line represents the unity line corrected for the negative bias of 1.8 mm ( $y = x - 1.8$ ).

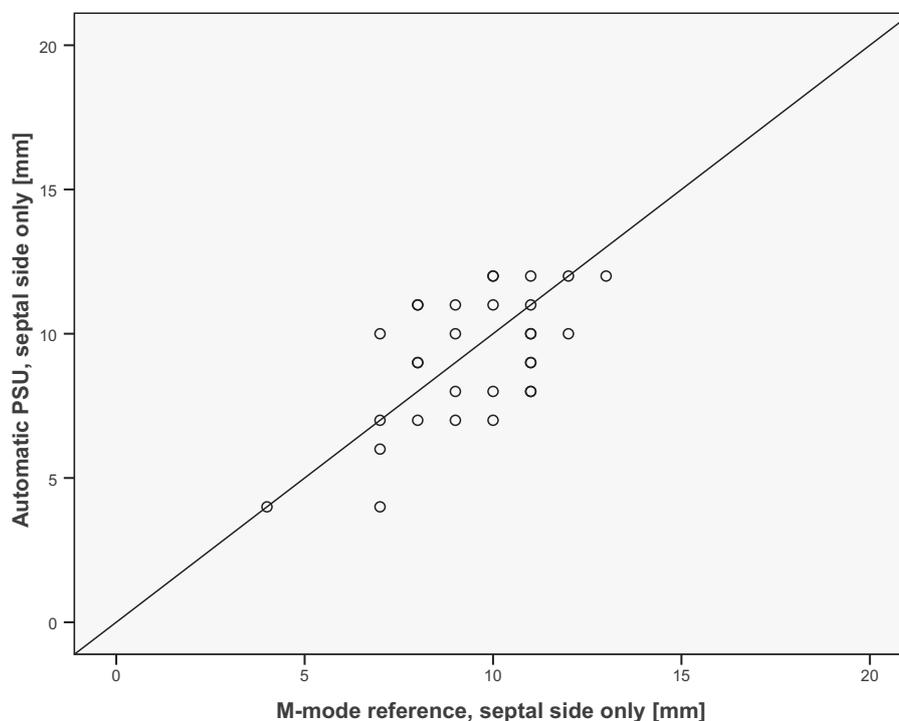


Fig. 7. Scatter plot with the PSU results using only the septal value along the vertical axis and the septal m-mode reference values along the horizontal axis. The solid line is the reference unity line ( $y = x$ ).

- The combination should be a smooth process to avoid jumps and discontinuities in the result.

The chosen solution is to use a weighted sum of  $\mathbf{x}_{i,K}$  and  $\mathbf{x}'_{i,S}$ :

$$\mathbf{x}_{i,S} = a * \mathbf{x}_{i,K} + (1-a) * \mathbf{x}'_{i,S}. \quad (3)$$

The weighting function  $a$  is chosen as an exponential function

$$a = \min\{\exp(C * (\|\mathbf{x}_{i,K} - \mathbf{x}'_{i,S}\| - T)), 1\}. \quad (4)$$

The constant  $C$  has been set to 650 and  $T$  is selected to be 0.010. The resulting weighting function is displayed in Fig. 2. Using this setup, it can be seen that as long as the difference between the Kalman filter and speckle tracker-defined points is  $< 5$  mm, the process is controlled mainly by the speckle tracker. When approaching a difference of 1 cm, the weight is rapidly but smoothly shifted to the Kalman filter-based values. After 1 cm, the new kernel positions are solely defined by the Kalman filter segmentation.

The tracking process is repeated for all frames  $[i+1, i+2, \dots]$ .

#### MAE value

The coordinates of the tracking points  $\mathbf{x}_{i,S}$  are used to find MAE. Using the deformable model, a unity vector,  $\mathbf{n}_{ap}$ , pointing from the center of the AV plane to the cardiac apex is calculated. Taking the inner product of this vector and the average position of the two tracking points yields a distance measure for the mitral annulus toward the apex,  $y_{MAE}$ :

$$y_{MAE_i} = \langle \bar{\mathbf{x}}_{i,S}, \mathbf{n}_{ap} \rangle. \quad (5)$$

Considering one heart cycle only, the mitral annulus excursion is found to be  $MAE = \max\{y_{MAE_i}\} - \min\{y_{MAE_i}\}$ . Figure 3 shows a flowchart providing an overview of the overall tracking system.

#### Manual corrections

Although the algorithm is designed for automatic operation, some optional manual interaction is supported. This covers manual re-initialization of the tracking points and model position. In addition, the lateral tracking point can be disabled, which can be relevant in a few hard-to-image patients. We will present both fully automatic and semiautomatic results.

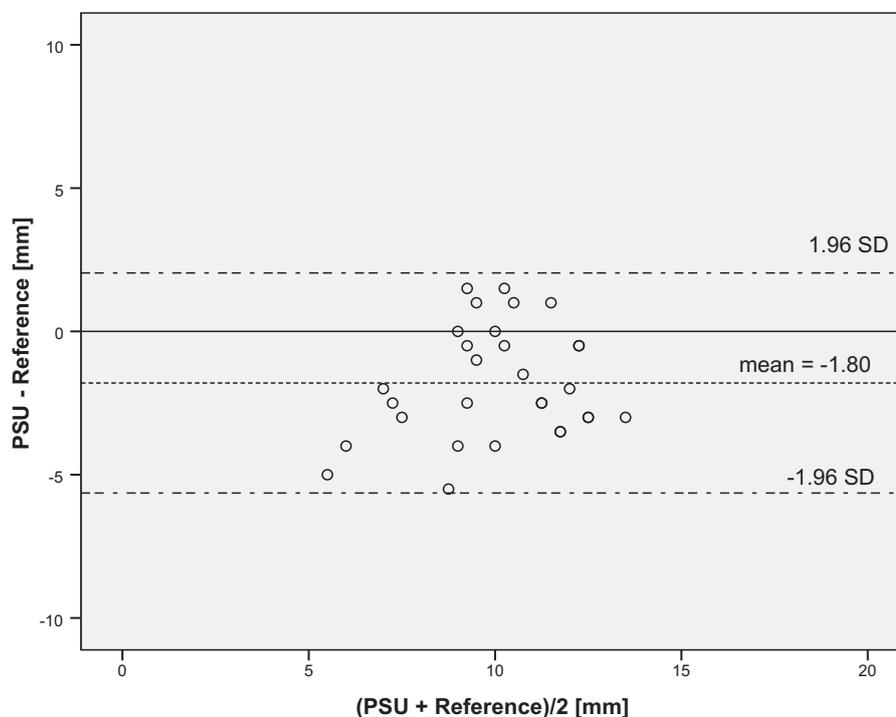


Fig. 8. Bland-Altman plot of the measurement difference between the automatic algorithm using PSU and manual m-mode measurement on HCU data. The dashed line represents the bias in the data, whereas the dash-dotted lines represent the 95% limits of agreement.

#### Acquisition of data

The algorithm was tuned using recordings from a PSU scanner (Vscan, GE Vingmed Ultrasound, Horten, Norway) and a commercially available high-end scanner (Vivid 7, GE Vingmed Ultrasound). Test data were acquired from 30 patients (age  $72.8 \pm 10.8$  y; 60% men) who previously either had suffered a myocardial infarction or had known systolic heart failure or known arterial hypertension. An ethical committee approval was obtained, and informed consent for the study was obtained from all human subjects per the WORLD Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects. A cardiologist collected the data from the apical four-chamber view using a commercially available laptop scanner (Vivid i, GE Vingmed Ultrasound) and a PSU system (Vscan, GE Vingmed Ultrasound). Following American Society of Echocardiography (ASE) nomenclature (Seward *et al.* 2002), the laptop scanner is in the following denoted as the HCU device, even if the image quality and user interface of this particular HCU device is close to that of a full-size scanner.

#### Analysis

The cardiologist measured MAE on the HCU data using anatomic m-mode in the EchoPac software package (GE Vingmed Ultrasound). Both the septal and lateral sides were measured. One HCU recording was considered unsuitable for speckle tracking and was therefore excluded from the analysis. The algorithm was thus tested on 30 patients from the PSU device and 29 patients from the HCU system.

The algorithm was tested offline on a standard laptop computer. The fully automatic solution was tested by running the algorithm using a batch script. One complete cardiac cycle must be analyzed to calculate MAE. In addition, the Kalman filter must have converged before initializing the speckle-tracking points. This normally occurs within the first 10 frames. For convenience, each recording was run for two complete cycles. At the end of the second cycle, the MAE value was automatically stored together with an image and movie of the tracking. We tested both to use the septal point separately and to use the average of the septal and lateral points for calculating the MAE value. The analysis was run using both PSU and HCU data.

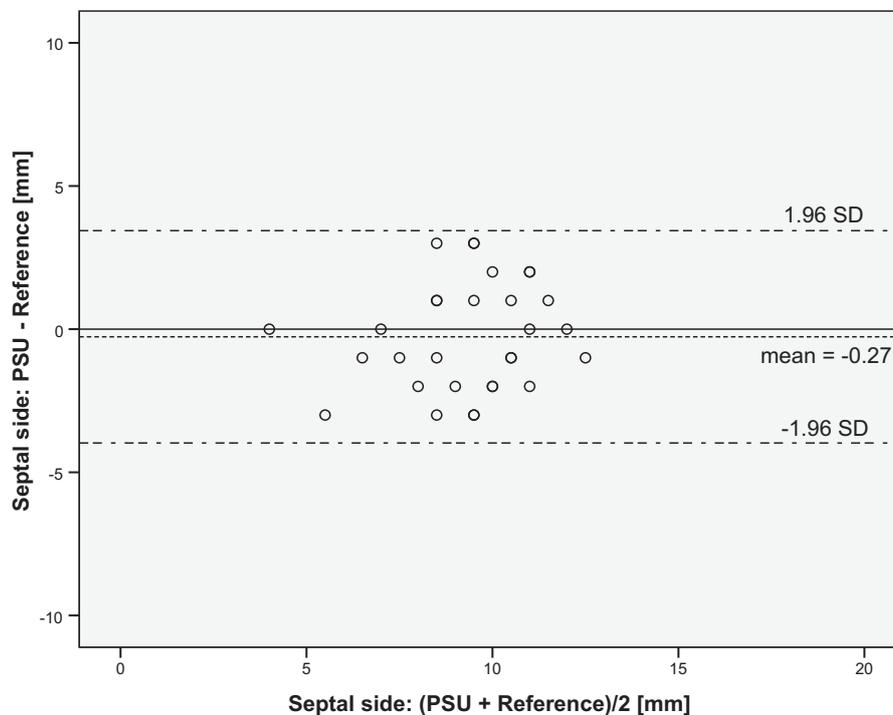


Fig. 9. Bland-Altman plot of the measurement difference between the automatic algorithm using only the septal point and PSU and manual m-mode measurement on HCU data. The dashed line represents the bias in the data, whereas the dash-dotted lines represent the 95% limits of agreement.

Semiautomatic operation was tested by allowing a second cardiologist, blinded to the reference measurements, to operate the algorithm while allowing for manual corrections. Semiautomatic operation using the septal point only was not tested. However, because the clinician had the option of manually turning off the lateral point, some of the reported semiautomatic MAE values were in reality based on medial tracking only. In these cases, we chose not to adjust the reference value accordingly. This has the consequence that in cases where the semiautomatically reported MAE value in reality was based on the septal excursion only, the reference value was still defined as the average of the lateral and septal anatomic m-mode measurements. The cardiologist noted what changes he made and rated the image quality as “good” or “poor.” The image quality was rated good in 19 (61.3%) cases using PSU and in 20 (69.0%) cases using HCU.

After testing for normality, the automatic results and the anatomic m-mode references were compared using paired *t*-test and Pearson’s correlation coefficient. Bland-Altman plots and scatter plots of the results were produced.

The mean and maximum absolute errors were calculated. The null hypothesis was that there was no difference between the automatic method and the manual m-mode reference. To assess the value of user interaction, the results from the semiautomatic analysis were also analyzed.

## RESULTS

Two examples of excursion measurements, one from the PSU and one from the HCU system, are shown in Figs. 4 and 5. The results from the automatic and semiautomatic analysis are presented in Table 1. Figures 6 and 7 present scatter plots for the PSU device using, respectively, both points and the septal point only. Bland-Altman plots are provided in Figs. 8 and 9. For the HCU device, scatter plots are found in Figs. 10 and 11, whereas Bland-Altman plots are found in Figs. 12 and 13. For the semiautomatic analysis using PSU data, the cardiologist let the algorithm process 15 of the 30 recordings fully automatic. For the HCU data, only five of the 29 were processed fully automatic. The manual corrections are summarized in Table 2.

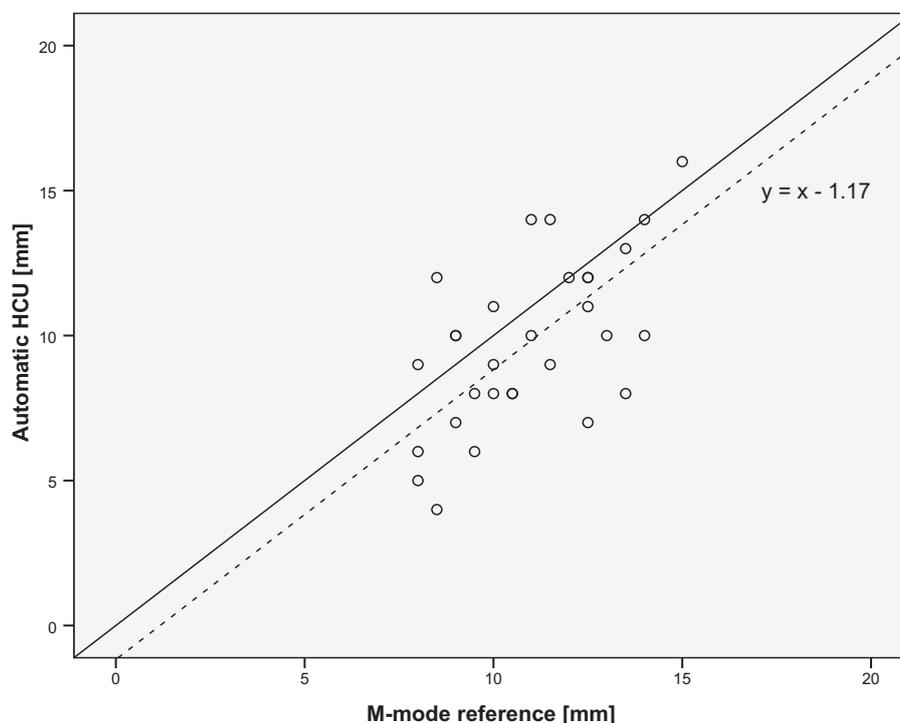


Fig. 10. Scatter plot with the HCU results along the vertical axis and the m-mode reference values along the horizontal axis. The solid line is the reference unity line ( $y = x$ ). The dashed line represents the unity line corrected for the negative bias of 1.17 mm ( $y = x - 1.17$ ).

The Kalman tracking used on average 2.5ms/frame and the speckle tracking 1.2 ms/frame on a regular laptop computer (1.17 GHz dual-core, 2 GB RAM). The frame rate for the PSU data was on average 20 fps and 55 fps for the HCU data.

### DISCUSSION

The results from the analysis of PSU data suggest that fully automatic assessment of MAE using a PSU scanner is feasible. The lateral tracking is most challenging. When the average of the septal and lateral excursions is used to calculate MAE, the lateral point introduces a negative bias of 1.8 mm. By tracking the septal point only, the negative bias is reduced to 0.27 mm and is no longer statistically significant. This is similar to the results of Hayashi *et al.* (2006), who reported a statistically significant difference of (mean  $\pm$  SD)  $1.94 \pm 3.96$  mm between anatomic m-mode measurements and speckle tracking on the lateral side. They did not find significant bias on the septal side. We found the 95% confidence interval of the error to be

$-2.53$  to  $-1.07$  mm when using both points and a narrower  $-0.97$  to  $0.44$  mm when only using the septal point. The maximum absolute error was reduced from 5.5 to 3 mm when only the septal point was used. The poor lateral tracking is probably caused by inferior image quality on the lateral side, which often suffers from dropouts and out-of-plane motion.

Judging from the results, the algorithm performance seems less sensitive to frame rate. By using HCU data, the overall results improved slightly, but because of the higher frame rate, a larger improvement was expected. Several of the HCU images had very high gain in the base. This caused saturation and poor visibility of the speckle pattern. Unfortunately, the saturation was also present in the raw data, so the problem could not be resolved offline. This may have influenced the tracking performance when the algorithm was used with HCU data.

When the algorithm was operated semiautomatically, the operator frequently corrected both the model and tracking point initialization. Only 50% of the PSU recordings and 17% of the HCU recordings were

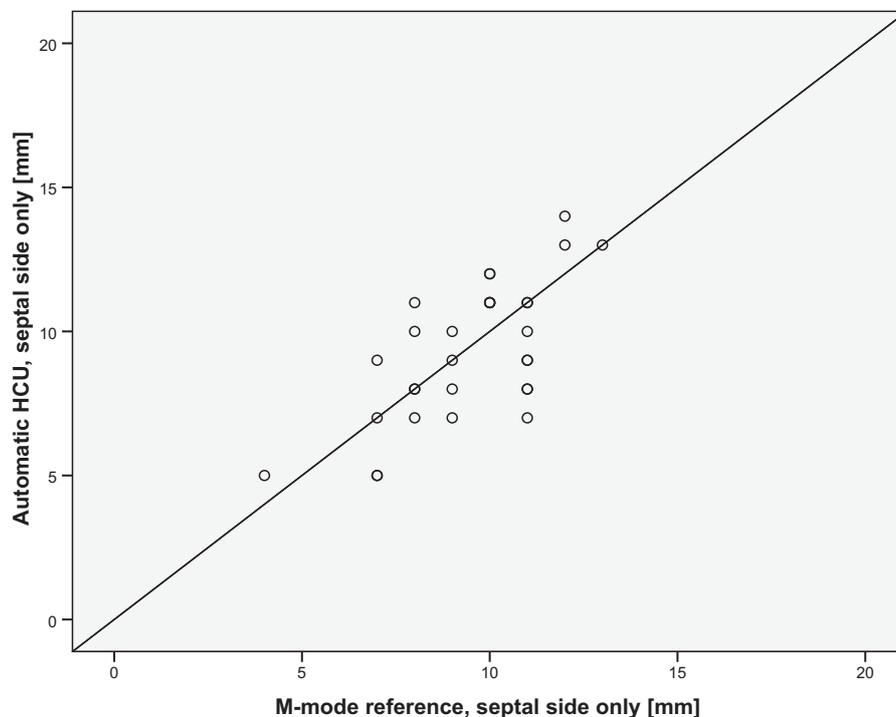


Fig. 11. Scatter plot with the HCU results using only the septal value along the vertical axis and the septal m-mode reference values along the horizontal axis. The solid line is the reference unity line ( $y = x$ ).

processed without interaction. The most frequent corrections for the PSU data were disabling the lateral point (23%) and correction of the septal point (24%). For the HCU data, both the lateral and septal points were frequently adjusted. The lateral point was disabled in 24% of the cases. In case of HCU data, the frequent repositioning of the tracking points can be partly explained by the gain problems in the base, because the clinician was instructed to move tracking points away from saturated regions. The correction process was very straightforward, only using two mouse clicks. It may be that the clinician did more of an optimization than a correction of the tracking points. This is supported by the limited gain from the user interaction. By introducing manual interaction, the maximum error was reduced from 5.5 to 4.5 mm for the PSU device and from 5.5 to 4 mm for the HCU device. It also registered a small reduction in the mean absolute error (0.2 mm for PSU and 0.3 mm for HCU data) and the standard deviation of the error. It seems that the main effect of manual interaction is reduction of outliers. It is questionable whether the minor improvements can justify manual interaction when implemented on a PSU device.

The correlation coefficients range from  $r = 0.61$  to  $r = 0.69$  and are statistically significant. Hayashi et al. (2006) reported a  $r^2 = 0.55$  ( $r = 0.74$ ) correlation between anatomic m-mode and speckle tracking for the septal side and a nonsignificant value for the lateral side. This is comparable with our results. We believe that the correlation coefficients would benefit from having data with a wider range in the excursion values. Our set has a value range from 6–14 mm. Eto et al. (2005) presented values ranging from 1.9–24.6 mm and achieved a correlation of  $r = 0.86$  when comparing their semiautomatic speckle-tracking approach with manual atrioventricular plane tracing in 3-D echo. They also reported a difference of (mean  $\pm$  SD)  $2.5 \pm 1.8$  mm compared with the manual tracing.

The standard deviation of the error is relatively high, which can also be seen from the Bland-Altman plots. This is caused by several things. The size of the dataset is limited, and the patients were not from a healthy population. All patients had a previous history of myocardial infarction, known hypertension or systolic heart failure. The image quality was on the low side of the quality scale. The cardiologist judged 38.7% of the PSU

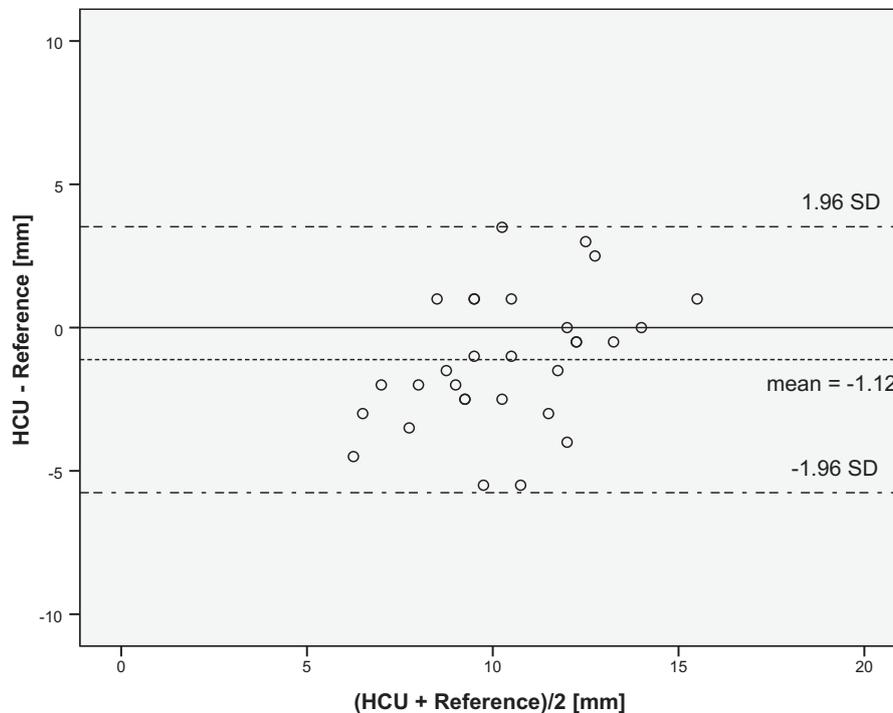


Fig. 12. Bland-Altman plot of the measurement difference between the automatic algorithm and manual m-mode measurement. Both the automatic results and reference measurements were made using HCU data. The dashed line represents the bias in the data, whereas the dash-dotted lines represent the 95% limits of agreement.

recordings and 31.0% of the HCU recordings as having “poor” image quality. Because the patients were mostly  $>60$  years of age, use of a conversion factor of 5 between MAE and EF (Emilsson and Wandt 2000) translates the standard deviation of the error to 9.8% for automatic PSU analysis and 11.6% for automatic HCU analysis, in terms of EF. By only using the septal point for MAE calculation, the numbers are 9.5% (PSU) and 8.9% (HCU). The review paper by McGowan and Cleland (2003) reported interobserver variabilities of EF using Simpson’s rule, corresponding to standard deviations of the difference between the observers, ranging from 4.1% (a study on echogenic patients) to 10.7%. For intra-observer variability, the range was 3.1–6.6%. The algorithm does not perform much worse as an EF estimator than these reported numbers, even if these are studies with full-size scanners.

Nevo *et al.* (2007) presented a semiautomatic method for MAE measurement using low-frame-rate (25 Hz) images. The disadvantage of this solution is the reported long computation time of (mean  $\pm$  SD)  $162.1 \pm 10.3$  s. A PSU scanner operating at 20 fps has a 50-ms-per-frame time limit for real-time algorithm

operation. The computation time of our algorithm was 3.7 ms per frame and suggests that a real-time PSU implementation is feasible, provided that the computational capacity of the PSU systems is approaching that of a regular laptop computer. This will further speed up the examination and completely avoid the need for post-processing.

#### Limitations and future work

The goal of this work was to assess left ventricular systolic function by measurement of MAE using a PSU device. It was chosen to use manual anatomic m-mode-based MAE measurements as the reference. An alternative would be to use EF. For instance, DeCara *et al.* (2005) presented a study based on Philips QLab, where they achieved a close correlation ( $r^2 = 0.72$ ) between semiautomatic MAE and biplane EF, using multiple regression. A similar study using Philips Qlab was presented by Tsang *et al.* (2010). Different regression formulas have also been presented in several other publications (Emilsson *et al.* 2000; Eto *et al.* 2005). Unfortunately, there does not seem to be general agreement on which regression formula to use. In this

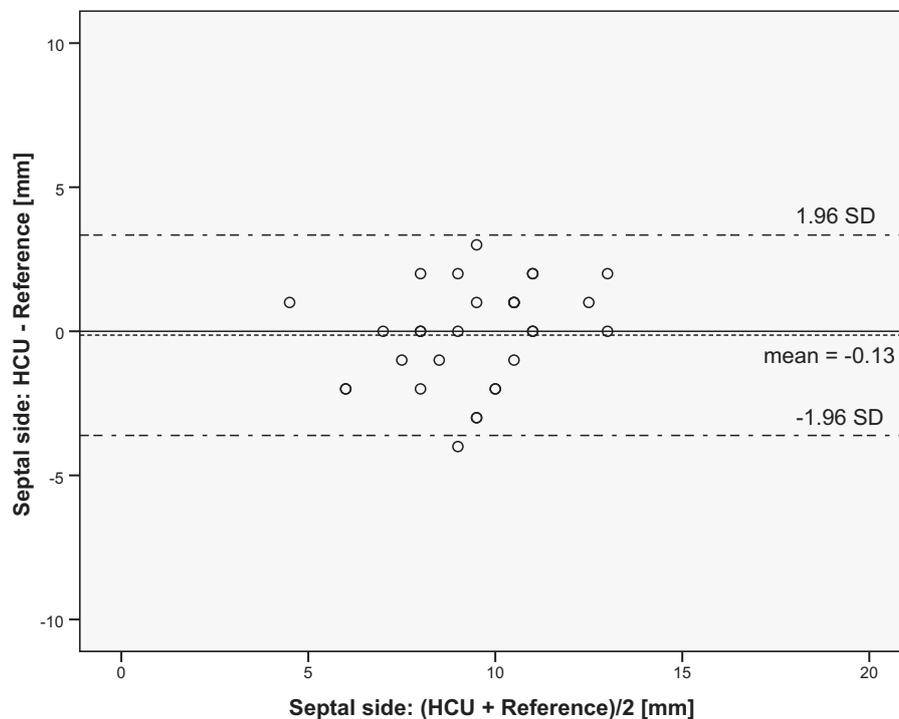


Fig. 13. Bland-Altman plot of the measurement difference between the automatic algorithm using only the septal point and manual m-mode measurement. Both the automatic results and reference measurements were made using HCU data. The dashed line represents the bias in the data, whereas the dash-dotted lines represent the 95% limits of agreement.

work, it was thus chosen to use manual MAE directly as the reference. This can be seen as a limitation, because many still consider EF to be the gold standard when measuring cardiac systolic function.

MAE is often measured in several projections and the MAE value is reported as the average excursion. In this work, only the apical four-chamber view has been used. Also, the best automatic results were achieved using the septal point only. This solution is sensitive to local variability in the excursion of the mitral annulus, for instance, caused by an infarction.

The tested HCU recordings suffered from gain and saturation issues. This may have influenced the HCU results. For the PSU device, the spatial resolution may have been limited by its output format, which was Cartesian image of  $240 \times 320$  pixels.

Our algorithm is intended to be operated also by less experienced users. In this work, the recordings were made by a cardiologist. This is a limitation, because the image quality is likely to be worse when the operator is not an expert. The number of subjects in the feasibility study is also limited. A larger clinical validation study should

be conducted with data from a broader population and, preferably, should include users with limited training.

Although our computation times suggest that a real-time implementation of the method on a PSU device is feasible, we have not been able to physically verify this. A real-time implementation on a PSU device should be pursued.

To make the method more accurate, improvements of the lateral tracking is important. Future work should aim to improve the accuracy of the model fit, for example,

Table 2. Table listing the manual corrections performed during semiautomatic analysis using the 30 PSU recordings and the 29 HCU recordings

	PSU	HCU
Uncorrected cases, n (%)	15 (50%)	5 (17%)
Lateral point disabled cases, n (%)	7 (23%)	7 (24%)
Lateral point adjusted cases, n (%)	4 (13%)	10 (34%)
Septal point adjusted cases, n (%)	8 (27%)	12 (41%)
Model adjusted vertically cases, n (%)	3 (10%)	6 (21%)
Model adjusted horizontally cases, (%)	3 (10%)	4 (14%)

by developing new edge detectors and improvements to the parametric left ventricle model. By putting more weight on the model motion than the block matching, the lateral mitral annulus tracking could possibly be made more accurate.

## CONCLUSIONS

We have presented a fully automatic algorithm for MAE measurement using low-frame-rate, apical four-chamber images from a PSU device. The algorithm is highly efficient, and the measured computation times strongly suggest that real-time operation is feasible. The accuracy of the algorithm should be suitable for successfully separating poor ventricles from normal ones and is comparable with previously reported numbers comparing anatomic m-mode and semiautomatic regular frame-rate speckle tracking. The MAE values are on average underestimated. This effect is reduced by only using the septal point for MAE calculation. We believe that the presented algorithm is a promising method for rapid assessment of systolic function using PSU systems.

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## APPENDIX A

### TECHNICAL NOTES—MODEL-BASED SEGMENTATION

This appendix covers the detailed description of the model-based segmentation algorithm, using a Kalman filter.

#### Calculating model points

The parametric model used in this work is based on NURBS. This is a generalization of the commonly used B-splines. A  $k$ 'th degree NURBS curve is defined by:

$$\mathbf{p}_i(u) = \frac{\sum_{j=0}^n N_{i,k}(u) w_j \mathbf{q}_j}{\sum_{j=0}^n N_{i,k}(u) w_j}, \quad a \leq u \leq b, \quad (\text{A1})$$

where  $N_{i,k}(u)$  are the  $k$ 'th-degree B-spline basis functions,  $\mathbf{q}_j$  are the control points for the spline. Lastly,  $w_j$  are the weights of the NURBS

curve. The constants  $a$  and  $b$  are upper and lower bounds for the parametric coordinate,  $u$ . We denote points on the NURBS curve as  $\mathbf{p}_l(u)$  for reasons that will become clear later. We define the rational basis functions as:

$$b_{i,k}(u) = \frac{N_{i,k}(u)w_i}{\sum_{j=0}^n N_{j,k}(u)w_j}, \quad a \leq u \leq b, \quad (\text{A2})$$

which allows us to write:

$$\mathbf{p}_l(u) = \sum_{i=0}^n b_{i,k}(u) \mathbf{q}_i, \quad a \leq u \leq b. \quad (\text{A3})$$

The basis functions are defined on the knot vector:

$$U = a, \dots, a, u_{k+1}, \dots, u_{m-k-1}, b, \dots, b. \quad (\text{A4})$$

We note that the NURBS curves are linear in their control points, which make them well suited for parameter estimation. In this work, the knot vector has been chosen such that  $a = 0, b = 1$  and  $u_{k+1}, \dots, u_{m-k-1}$  are uniformly distributed. The left ventricle model is designed in a custom-made MATLAB (v2008a, The MathWorks, Inc., Natick, MA, USA) environment, where it is possible to freely select control points, knots, weights and parametric coordinates for edge and speckle-tracking measurements. The weights have been adjusted to preserve the corner between the AV plane and the LV walls.

### System states

A Kalman filter requires the model or system to be described by states. We choose to denote the normal displacement of the control vertices as the local states,  $\mathbf{x}_l$ . The control point is written as:

$$\mathbf{q}_i = \bar{\mathbf{q}}_i + x_{i,n} \mathbf{n}_i, \quad (\text{A5})$$

where  $\mathbf{n}_i$  is the normal displacement vector for the control vertex and  $\bar{\mathbf{q}}_i$  is the mean position of the control vertex. The pose parameters (translation, rotation and scale) are used as global states,  $\bar{\mathbf{x}}_g$ . Combining the local and global states results in one state vector suitable for the Kalman filter framework,  $\mathbf{x} = \mathbf{x}_l + \mathbf{x}_g$ . Control points in the base center should not be moved because no significant shape alternations are expected in this region. These points are thus not included in the state vector.

The relation between the system states and the points on the deformable model is described by a local ( $T_l$ ) and global transform ( $T_g$ ). We denote the points on the final contour as  $\mathbf{p}$ . For simplicity, we write the points on the contour before application of the global pose as  $\mathbf{p}_l$ . We define a vector  $\mathbf{u}$  with length  $N_c$ , where  $0 \leq u_i \leq 1$ . This yields:

$$\mathbf{p}_l = [p_l(u_0), p_l(u_1), \dots, p_l(u_{N_c-1})], \quad (\text{A6})$$

where  $p_l(u_i)$  is evaluated using eqn (A.3) for each element in  $\mathbf{u}$ . Equation (A.3) thus defines the local transformation  $T_l$ .  $\mathbf{p}_l$  is then transformed by the global pose transform,  $T_g$  to obtain the correct position of the model.

$$\mathbf{p} = T_g(\mathbf{p}_l, \bar{\mathbf{x}}_g). \quad (\text{A7})$$

The composite deformation model,  $T$  includes both the local and global transforms. It is necessary to calculate the Jacobian of  $T$ . The local Jacobian matrix is found by multiplying the displacement vectors with their respective basis functions:

$$\mathbf{J}_l = [b_{i_0} \mathbf{n}_{i_0}, b_{i_1} \mathbf{n}_{i_1}, \dots]. \quad (\text{A8})$$

This can be precomputed, and thus eases the real-time operation.

The global  $T_g$  transform is directly applied to curve points, as in eqn (A.7). This is not the case with the curve normals, where the curve normal transformation rule must be applied (Orderud and Rabben 2008; Barr 1984):

$$\mathbf{n}_g = \left| \frac{\partial T_g(\mathbf{p}_l, \bar{\mathbf{x}}_g)}{\partial \mathbf{p}_l} \right| \left( \frac{\partial T_g(\mathbf{p}_l, \bar{\mathbf{x}}_g)}{\partial \mathbf{p}_l} \right)^{-T} \mathbf{n}_l. \quad (\text{A9})$$

The overall Jacobian matrix is derived applying the chain rule of multivariate calculus:

$$\mathbf{J}_g = \left[ \frac{\partial T_g(\mathbf{p}_l, \bar{\mathbf{x}}_g)}{\partial \bar{\mathbf{x}}_g}, \frac{\partial T_g(\mathbf{p}_l, \bar{\mathbf{x}}_g)}{\partial \mathbf{p}_l} \mathbf{J}_l \right]. \quad (\text{A10})$$

### Prediction step

During the prediction step, the state estimates are predicted based on the posterior estimates from the last iteration. It is also possible to expand this model-to-model motion. We use a bar above the variable to indicate the *a priori* value and a hat for the posterior value.

$$\bar{\mathbf{x}}_{k+1} - \mathbf{x}_0 = \mathbf{A}(\hat{\mathbf{x}}_k - \mathbf{x}_0). \quad (\text{A11})$$

### Measurements

Regarding measurement input to the Kalman filter, we have used simple edge measurements and block matching. The edge measurements are made using *normal displacements*.  $N_e$  edge points are distributed around the NURBS model. For each edge point, it is searched for an intensity transition along a normal,  $\mathbf{n}$ , to the NURBS curve in this point. We use a *step* detector based on minimization of the sum of square errors (SSE) between a perfect step function and the sample vector taken normal to the model. Weak edges are discarded using a thresholding of the intensity difference across the detected edge or the distance from the neighboring edge detector results. The distance from the edge point to the measured edge point is called a *normal displacement* measurement,  $v$ . The inverse of the mean intensity difference across the detected edge point is used as a measure of edge confidence,  $r$ .

$$v = \mathbf{n}^T (\mathbf{p}_{obs} - \mathbf{p}). \quad (\text{A12})$$

This measurement must be projected to state space, to be useful for the state update. The measurement model must be linear to fit in the Kalman filter framework. This is done using the normal vector projection of the Jacobian.

$$\mathbf{h}^T = \mathbf{n}^T \mathbf{J}. \quad (\text{A13})$$

The normal displacement measurements are thus now related to the state vector through  $\mathbf{h}^T$ . This implies a separate measurement vector,  $\mathbf{h}$  for each normal displacement measurement.

In addition to the edge measurements, block matching has been used as *Kalman filter input*.  $N_b$  points on the NURBS model are selected as centers for the block-matching blocks. In frame  $k$ , a single kernel block is extracted around each center point. In frame  $k+1$ , a kernel block of the same size is moved within a search window centered around the model center point from the previous frame, and a SAD fit to the previous frame is calculated, defining the new kernel center position for frame  $k+1$ . The normal component of the vector from the kernel position in frame  $k$  to frame  $k+1$  defines a normal displacement vector, and is used as a filter input in the same manner as for edge detection. This use of block matching is not strictly necessary, but adds to the robustness of the method.

### Assimilation

Calculating the regular Kalman gain using the standard equations will in this case be computationally intensive because there are many more measurements than there are states. The measurements are thus instead assimilated into *information space*. If the measurements can be considered uncorrelated, this gives a very efficient processing because the measurement covariance matrix,  $\mathbf{R}$ , becomes diagonal:

$$\mathbf{H}^T \mathbf{R}^{-1} \mathbf{v} = \sum_i \mathbf{h}_i r_i^{-1} v_i, \quad (\text{A14})$$

$$\mathbf{H}^T \mathbf{R}^{-1} \mathbf{H} = \sum_i \mathbf{h}_i r_i^{-1} \mathbf{h}_i^T. \quad (\text{A15})$$

This avoids inversion of matrices with dimension larger than the dimension of the state vector.

#### *Update*

The Kalman gain,  $\mathbf{K}_k$ , is given by:

$$\mathbf{K}_k = \hat{\mathbf{P}}_k \mathbf{H}^T \mathbf{R}^{-1}, \quad (\text{A16})$$

where  $\mathbf{P}$  means the error covariance matrix.

The update step becomes:

$$\hat{\mathbf{x}}_k = \bar{\mathbf{x}}_k + \hat{\mathbf{P}}_k \mathbf{H}^T \mathbf{R}^{-1} \mathbf{v}_k. \quad (\text{A17})$$

The updated error covariance matrix using information space becomes:

$$\hat{\mathbf{P}}_k^{-1} = \bar{\mathbf{P}}_k^{-1} + \mathbf{H}^T \mathbf{R}^{-1} \mathbf{H}. \quad (\text{A18})$$

By applying eqns (A.3), (A.7) and (A.5), it is now possible to calculate the model points.



# Paper III





# Feasibility and reliability of point-of-care pocket-size echocardiography performed by medical residents

Ole Christian Mjølstad<sup>1,2\*</sup>, Garrett Newton Andersen<sup>1,3</sup>, Håvard Dalen<sup>1,3</sup>,  
Torbjørn Graven<sup>3</sup>, Kyrre Skjetne<sup>3</sup>, Jens Olaf Kleinau<sup>3</sup>, and Bjørn Olav Haugen<sup>1,2</sup>

<sup>1</sup>MI Lab and Department of Circulation and Medical Imaging, Norwegian University of Science and Technology, Postboks 8905, Trondheim 7491, Norway; <sup>2</sup>Department of Cardiology, St Olav, Trondheim University Hospital, Prinsesse Kristinas gate 3, Trondheim 7006, Norway; and <sup>3</sup>Levanger Hospital, Nord-Trøndelag Health Trust, Levanger 7600, Norway

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<b>Aims</b>	To study the feasibility and reliability of pocket-size hand-held echocardiography (PHHE) by medical residents with limited experience in ultrasound.
<b>Methods and results</b>	A total of 199 patients admitted to a non-university medical department were examined with PHHE. Six out of 14 medical residents were randomized to use a focused protocol and examine the heart, pericardium, pleural space, and abdominal large vessels. Diagnostic corrections were made and findings were confirmed by standard diagnostics. The median time consumption for the examination was 5.7 min. Each resident performed a median of 27 examinations. The left ventricle was assessed to satisfaction in 97% and the pericardium in all patients. The aortic and atrioventricular valves were assessed in at least 76% and the abdominal aorta in 50%, respectively. Global left-ventricular function, pleural, and pericardial effusion showed very strong correlation with reference method (Spearman's $r \geq 0.8$ ). Quantification of aortic stenosis and regurgitation showed strong correlation with $r = 0.7$ . Regurgitations in the atrioventricular valves showed moderate correlations, $r = 0.5$ and $r = 0.6$ for mitral and tricuspid regurgitation, respectively, similar to dilatation of the left atrium ( $r = 0.6$ ) and detection of regional dysfunction ( $r = 0.6$ ). Quantification of the abdominal aorta (aneurysmatic or not) showed strong correlation, $r = 0.7$ , while the inferior vena cava diameter correlated moderately, $r = 0.5$ .
<b>Conclusion</b>	By adding a PHHE examination to standard care, medical residents were able to obtain reliable information of important cardiovascular structures in patients admitted to a medical department. Thus, focused examinations with PHHE performed by residents after a training period have the potential to improve in-hospital diagnostic procedures.
<b>Keywords</b>	Echocardiography • Pocket-size • Hand-held • Point-of-care ultrasound • Bedside • Non-expert

## Introduction

An early and correct diagnosis is a crucial step in the treatment of patients. A delayed or wrong diagnosis may delay the treatment, complicate inpatient workflow, and may in worst case scenario have a lethal outcome.<sup>1</sup>

During the recent two decades, the development of new digital technology and miniaturization of ultrasound scanners have moved these scanners from the echo-labs into the white coat pocket.<sup>2,3</sup>

This makes them an excellent clinical tool, available for any physician in different clinical settings as a point-of-care ultrasonography.<sup>4</sup>

These newly developed scanners have been studied in several clinical settings. In the hands of experienced users, pocket-size hand-held echocardiographic (PHHE) devices offer high-quality semi-quantitative assessment of cardiac structures, abdominal great vessels, and the pleural space at the physicians' point-of-care with a demonstrable clinical benefit.<sup>5–11</sup>

\* Corresponding author. Tel: + 47 970 34 285; Fax: + 47 72 82 83 72, Email: ole.c.mjolstad@ntnu.no

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Medical history-taking and physical examination of most patients are performed by the residents in the emergency departments or bed wards. Few of these are skilled in ultrasonography and given the cost and the availability of the PHHE devices, non-expert users will frequently have such technology available for diagnostic use. Thus, we aimed to study the feasibility and reliability of PHHE in the hands of medical residents after a targeted training period in cardiovascular ultrasound.

## Methods

### Study population

This prospective observational study included 199 patients admitted to the medical department at Levanger Hospital, Norway. The patients were included in the period 4 April to 23 June 2011. The examination was performed by six medical residents taking part in the study. At study start, 12 medical residents were employed at the department, and half of them were randomized to participate in the study. During the study, another two residents joined the department, but they did not participate in the study. The residents have in-house call 24×7. Thus, the six participating residents covered ~42% of the total period of inclusion. All emergency admissions during the time these six residents were on call were included in the study. There were no other criteria of inclusion. Only patients who did not consent to participate or did not stay long enough in the department to enable the necessary diagnostic procedures for the study were excluded. Due to logistic reasons, inclusion of patients was restricted to 199 of 446 available patients as standard diagnostic procedures and treatment had first priority.

The patients were admitted to the emergency room in a standard way. After having been triaged according to their symptoms, they were examined by the resident. Based on the medical history, physical examination, and supplemental tests, a preliminary diagnosis was made. Thus, usual care diagnostics were done prior to the examination with PHHE. All patients had standard follow-up according to their symptoms and findings. Patients, in whom pathology was suggested either by PHHE or by the standard clinical care, were referred for relevant gold-standard diagnostic follow-up. To improve the reliability of the sensitivity and specificity of the data, approximately 10 negatively described PHHE examinations per resident were randomly selected by the study committee and referred for reference imaging procedures as well. The study was approved by the Regional Committee for Medical Research Ethics, and conducted according to the second Helsinki Declaration. All the patients gave their informed consent to participate in the study.

### Education of residents

The residents underwent a brief training program covering both the examination with PHHE and interpretation of the recordings. The program consisted of 4 h of lectures dealing with the theoretical basics and pitfalls of cardiovascular ultrasonography. Normal and pathological findings were demonstrated, and they were all provided with access to a virtual ultrasound-imaging library. All participating residents had a personal supervisor. Subsequently, the residents underwent 3 months of practical training, initially together with the supervisors in the echo-lab and in the radiology department, then using PHHE in the medical department with close connection to experienced ultrasonographers, having the opportunity to discuss their findings. They were encouraged to perform at least 100 examinations during the tutorial period. The actual numbers performed were median (interquartile range) 95 (80–225) examinations.

### Pocket-size echocardiographic examination

The residents performed the PHHE examinations using a Vscan (version 1.2; GE Vingmed Ultrasound, Horten, Norway). This device offers B-mode and colour flow (CF) imaging. The total weight is 390 g including the phased array probe with bandwidth of 1.7–3.8 MHz. It provides two dimensional (2D) imaging and real time colour-Doppler within a sector that has fixed size, but is movable throughout the 2D sector. An algorithm enables automatic storage and loop recording of a cardiac cycle without ECG signal.<sup>12</sup> Patient identification was performed by voice recording and the automatically assigned examination number. All images and recordings were saved on the device's micro-SD card and later transferred to a computer by commercial software (Gateway; GE Vingmed Ultrasound).

The pocket-size echocardiographic examinations were performed bedside, and when possible with the patients in the left-lateral decubitus position. The examinations included parasternal long- and short-axis views and apical four-chambers, two-chambers, and long-axis views. All views contained 2D and CF recordings. The patients were turned to supine position when examining the abdominal great vessels. The pleural space was recorded from supine or upright position. A standard examination protocol was used. Assessment of left- and right-ventricular function were done semi-quantitatively from the parasternal and apical positions, classified as normal/near normal, moderate, or severe dysfunction. The quantification was based on the systolic excursion of the atrioventricular plane for both ventricles. In addition, eye-balling of the left-ventricular ejection fraction as  $\geq 45$ , 30–45, or  $< 30\%$  corresponded to normal/near normal, moderate, or severe dysfunction, respectively. With respect to the assessment of right-ventricular function, dilatation of the ventricle and/or diastolic shift to the left of the intraventricular septum was also included in the judgement. Severe regional dysfunction was classified as present or not. Valvular pathology and dysfunction was classified semi-quantitatively as mild, moderate, or severe. Quantification of stenosis was based on the amount of calcification and the movement of the cusps/leaflets. Quantification of the regurgitations was based on the CF jet and size and function of the adjacent chambers. The size of the left atrium (LA) was measured online from the parasternal position and quantified as normal ( $< 40$  mm), moderately dilated (40–50 mm), or severely dilated ( $> 50$  mm). Pericardial effusion was if present classified as significant or not based on visual judgement of the influence of the adjacent chambers. The inferior vena cava diameter was assessed from the subcostal position at the end expiration within 2 cm from the right atrial orifice. The size of the abdominal aorta was determined by the largest measured diameter. It was classified as aneurysmatic if the diameter exceeded 30 mm. Both pleural cavities were examined. If pleural effusion was present, this was graded as small or large amount. A large amount of pleural effusion was registered if the diameter between the thoracic wall and the lung exceeded 5 and 4.5 cm in the left or the right pleural cavity, respectively. The examinations of the different structures were judged by the residents as feasible if they were able to quantify the specific cardiac structures or function indices based on their recordings.

### Validation of point-of-care pocket-size echocardiography

Standard echocardiography was performed in the hospital's echo-lab, under optimal conditions. The system used was a Vivid 7 scanner (GE Vingmed Ultrasound, Horten, Norway) using a 2.0 MHz phased-array transducer (M3S) with bandwidth 1.5–3.6 MHz. Second harmonic imaging was used. The recording of a cardiac cycle was ECG triggered. The standard examinations were performed independently by one

of four experienced cardiologists blinded to the results of PHHE with a median (range) time delay of 21.1 (0.4–166) h. A complete echocardiographic examination was performed. Dimensions were measured from a parasternal view. Ejection fraction was measured by Simpson's rule from apical four- and two-chamber views.<sup>13</sup> Valvular pathology was graded according to the recommendations from the European Association of Cardiovascular Imaging (EACVI) [former European Association of Echocardiography (EAE)].<sup>14–16</sup> For the analyses of the patients who underwent both echocardiographic and radiographic examinations, the radiologists' classifications of pleural effusion [computer tomography (CT) or ultrasound] and the size of the abdominal aorta were preferred.

### Statistical analysis

As the different echocardiographic and anthropometric measures partly were skewed compared with normal distribution, the basic characteristics are presented as mean  $\pm$  standard deviation (SD) and (interquartile) range. Spearman's rho ( $r$ ) was used for comparison of the ranking of pathology between the PHHE and the high-end echocardiographic examinations. Data are presented as  $r$  [95% confidence interval (CI)] with the 95% CI computed using bootstrapping. For comparison of continuous variables, Pearson's rho ( $r$ ) and Bland–Altman statistics were used. Statistical analyses were performed using SPSS for Windows version 20.0 (SPSS, Inc., Chicago, IL, USA).

## Results

### Study population

Table 1 shows the baseline data of the 199 patients included in the study (107 men and 92 women). Mean  $\pm$  SD (range) age was 65.6  $\pm$  18.2 (17.1–98.5) years. The distribution of age was positively skewed compared with a normal distribution. The mean

height was 170.9  $\pm$  9.7 cm and the body mass index was 26.4  $\pm$  5.6 kg/m<sup>2</sup>. At admission, atrial fibrillation was present in 33 (17%) patients, hypertension was present in 67 (34%) patients, 36 (18%) had known diabetes mellitus, and 20 (10%) had established heart failure. In total, cardiovascular disease defined as either angina pectoris, prior myocardial infarction, prior stroke, or established peripheral arterial disease was present in 71 (36%) of the patients. There were no significant differences in the basic characteristics of the 199 participants included in the study and the 247 participants not included in the study, but who were admitted to the hospital the days when the six residents performing PHHE examinations were on duty.

### Pocket-size hand-held echocardiography

The time consumption of the examination, including large vessels, was median (range) 5.7 (1.6–19.9) min. Each resident performed a median (interquartile range) of 27 (19–46) examinations. Table 2 shows the feasibility of PHHE. The left-ventricular (LV) function was assessed to satisfaction in nearly all of the patients (97%) and the pericardial space in all patients. The aortic and atrioventricular valves were assessed in at least 76% and the pulmonary valve in <50% of the patients. The vena cava inferior was assessed to satisfaction in 77% and the abdominal aorta in 50% of the population. This is also illustrated in Figure 1.

A total of 133 and 74 patients underwent high-end echocardiography and radiographic (CT or ultrasound) reference imaging, respectively. In total, 186 (93%) patients underwent reference imaging (Figure 2). For the different indices of cardiac structure or function, the available numbers of validated examinations are shown in Tables 3 and 4. Table 3 shows the correlations of semi-quantitative assessment of cardiovascular structures and function indices between PHHE and standard echocardiography. The classification of global left-ventricular function, pleural, and pericardial effusion showed very strong correlation with standard diagnostic procedures (Spearman's  $r \geq 0.83$ , with variations between residents 0.70–0.93, 0.54–1.0, and 0.81–1.0, respectively). Regional left-ventricular function showed moderate correlation,  $r = 0.60$  (variation between residents 0.53–0.61). The classification of

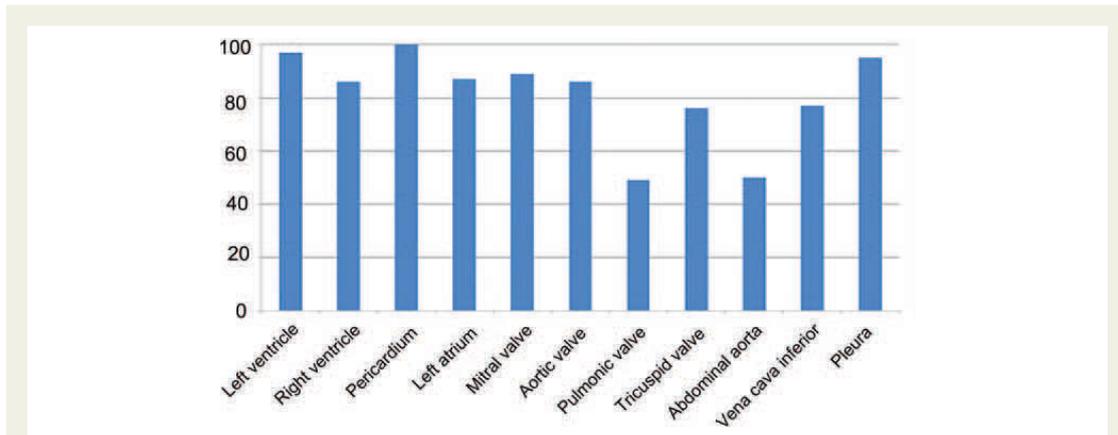
**Table 1 Basic characteristics of the 199 study participants**

	Mean $\pm$ SD (range) <sup>a</sup>
Age, years	65.6 $\pm$ 18.2 (17.1–98.5)
Male, $n$ (%)	107 (53.8)
Height, cm	170.9 $\pm$ 9.7 (150–196)
Body mass index, kg/m <sup>2</sup>	26.4 $\pm$ 5.6 (12–45)
Systolic blood pressure, mmHg	143.9 $\pm$ 28.6 (74–245)
Diastolic blood pressure, mmHg	75.0 $\pm$ 15.6 (24–120)
Heart rate, bpm	82.8 $\pm$ 22.6 (40–160)
Atrial fibrillation, $n$ (%)	33 (16.6)
Known hypertension, $n$ (%)	67 (33.7)
Known diabetes, $n$ (%)	36 (18.1)
Known myocardial infarction, $n$ (%)	32 (16.1)
Known angina, $n$ (%)	17 (8.5)
Known heart failure, $n$ (%)	20 (10.1)
Known peripheral vessel disease, $n$ (%)	7 (3.5)
Known stroke, $n$ (%)	35 (17.6)
Known cardiovascular disease, $n$ (%)	71 (35.7)
Known cancer, $n$ (%)	16 (8.0)

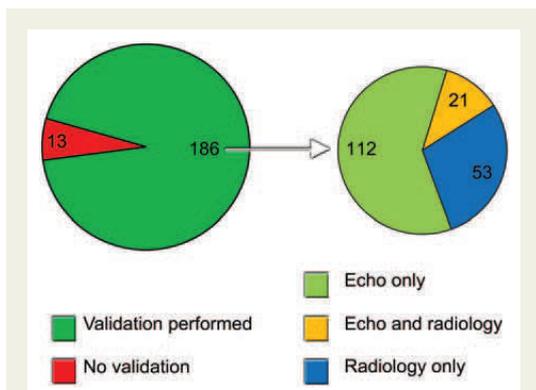
<sup>a</sup>Data are presented as mean  $\pm$  SD (range) unless otherwise specified.

**Table 2 Feasibility of point-of-care pocket-size echocardiography**

Anatomic structure	Assessed to satisfaction (%)
Left ventricle	194 (97)
Right ventricle	172 (86)
Pericardium	199 (100)
Left atrium	173 (87)
Mitral valve	177 (89)
Aortic valve	171 (86)
Pulmonary valve	97 (49)
Tricuspid valve	152 (76)
Abdominal aorta	99 (50)
Vena cava inferior	154 (77)
Pleura	190 (95)



**Figure 1** Feasibility of point-of-care pocket-size echocardiography. Feasibility (%) of the different cardiovascular structures when pocket-size echocardiography was performed by residents. The examinations of the different structures were judged by the residents as feasible if they were able to quantify the specific cardiac structures or function indices based on the recordings.



**Figure 2** Validation of PHHE. Illustration of the number of patients that were validated with reference imaging (left) and by what kind of reference imaging (right). Echo, echocardiography.

aortic valve calcification/stenosis and regurgitation showed strong correlation with  $r = 0.67$  (variation between residents 0.29–0.93) and  $r = 0.68$  (variation between residents 0.33–1.0), respectively. Regurgitation of the atrioventricular valves showed moderate-to-strong correlations,  $r = 0.53$  (variation between residents 0.34–0.80) for mitral and  $r = 0.61$  (variation between residents 0.21–0.78) for tricuspid regurgitation, so did the degree of dilatation of the LA ( $r = 0.61$ ) (variation between residents 0.23–0.76). No serious findings were missed. PHHE correlated strongly with standard diagnostics with respect to detect abdominal aortic aneurysms,  $r = 0.70$ . No aneurysms were missed, but there was one false positive diagnosis where the measurement of the aorta was 32 mm by PHHE and 28 mm by the abdominal CT. Figure 3 illustrates the

**Table 3** Correlations of semi-quantitative classification of echocardiographic indices of pocket-size echocardiography and reference method

	<i>n</i> total	<i>n</i> pathology	<i>R</i>	95% CI
Global systolic function, left ventricle	129	26	0.83	0.71–0.93
Apparent regional dysfunction, left ventricle	129	22	0.60	0.39–0.78
Global systolic function, right ventricle	115	10	0.44	0.10–0.72
Size of left atrium	117	68	0.61	0.48–0.72
Aortic calcification and stenosis	119	37	0.67	0.52–0.80
Aortic regurgitation	117	27	0.68	0.52–0.82
Mitral regurgitation	123	54	0.53	0.37–0.68
Tricuspid regurgitation	107	49	0.61	0.45–0.74
Pericardial effusion	131	4	0.86	0.57–1.00
Pleural effusion	151	20	0.83	0.67–0.94
Abdominal aorta	52	2	0.70	0.49–1.00
Inferior vena cava <sup>a</sup>	94		0.45	0.24–0.62

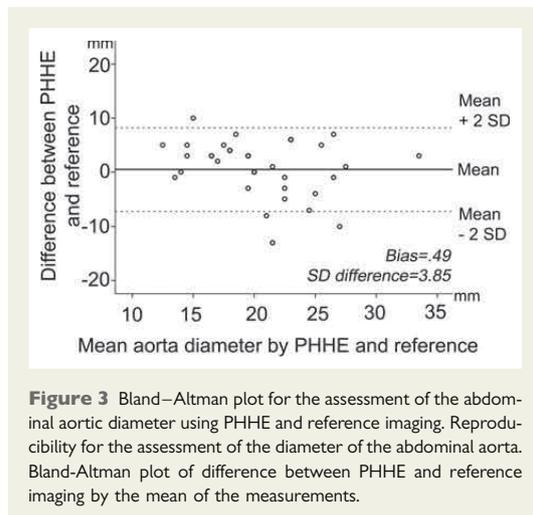
Data presented as correlation coefficient ( $r$ ) with 95% confidence interval achieved by bootstrapping. *n* total, the total number who underwent both PHHE and reference imaging; *n* pathology, total number with the described pathology. <sup>a</sup>Continuous variable, analysed by Pearson's correlation, all others analysed by Spearman's rank correlation.

reproducibility data of the abdominal aortic diameter. The maximal diameter of the inferior vena cava correlated only moderately with high-end echocardiography, Pearson's  $r = 0.45$ . Figure 4 illustrates the total number of misclassifications of global and regional

**Table 4** Sensitivity, specificity, positive, and negative predictive value of point-of-care pocket-size echocardiography to detect at least moderate pathology compared with reference method

	n total	n pathology	Sensitivity	Specificity	PPV	NPV
LV dysfunction	129	30	92	94	80	98
RV dysfunction	115	10	40	97	57	94
LA enlargement	117	68	62	94	93	64
Aortic regurgitation	117	27	82	89	69	94
Aortic stenosis/calcification	119	37	76	88	74	89
Mitral regurgitation	123	48	71	81	71	81
Tricuspid regurgitation	107	49	65	90	84	75

n total, the total number who underwent both PHHE and reference imaging; n pathology, total number with the described pathology; LV, left ventricle; RV, right ventricle; LA, left atrium; PPV, positive predictive value; NPV, negative predictive value.



**Figure 3** Bland–Altman plot for the assessment of the abdominal aortic diameter using PHHE and reference imaging. Reproducibility for the assessment of the diameter of the abdominal aorta. Bland-Altman plot of difference between PHHE and reference imaging by the mean of the measurements.

ventricular and valvular pathology by PHHE compared with the reference. For the quantification of LV global function, LA size, and aortic stenosis, respectively, 7, 2, and 5% of the misclassifications were two degrees; all other misclassifications were only one degree. *Figure 5* shows clinical examples of PHHE compared with reference method, and a clinical example is given in Supplementary material online, *Videos S1* and *S2*.

*Table 4* shows the sensitivity, specificity, positive, and negative predictive values of PHHE to detect at least moderate pathology. There was high specificity and negative predictive values of detecting left- and right-ventricular dysfunction and aortic-valve pathology. On the contrary, the lower sensitivity and positive predictive values for the assessment of right-ventricular function and left-atrial size are mainly caused by some underestimation of pathology.

## Discussion

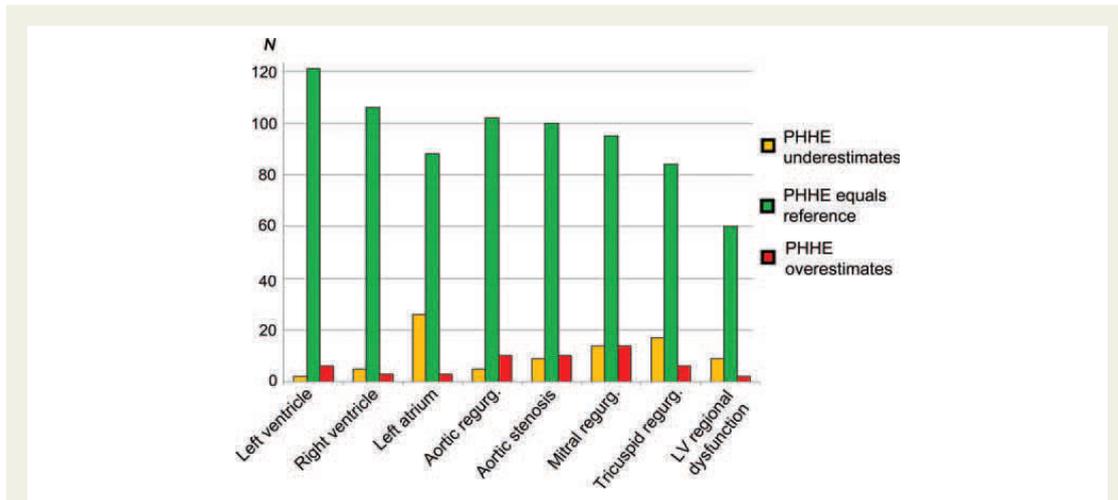
Our study demonstrates that medical residents in <6 min can perform a bedside ultrasound examination of the heart, pleural

space, and the abdominal great vessels after a 3 months training period and get reliable and clinically important diagnostic information beyond the standard physical examination.

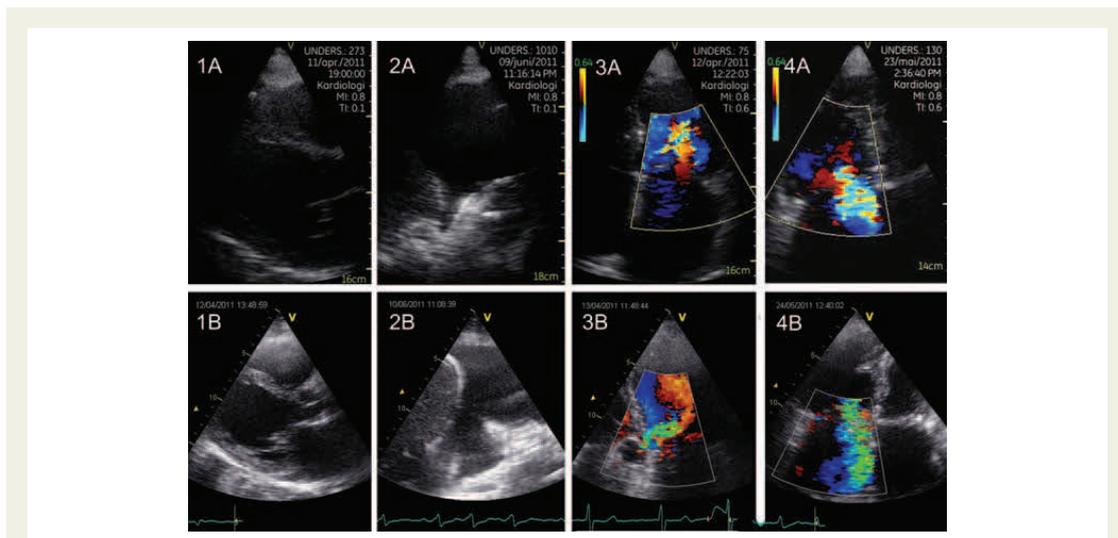
The patients were included solely during the time when the participating residents were on call and represent otherwise an unselected population in our department. The population characteristics are also in line with patient characteristics from previous studies in similar settings.<sup>10,17,18</sup>

PHHE has in several studies showed a high feasibility and accuracy when performed by experts.<sup>6–9</sup> Galderisi *et al.*<sup>8</sup> showed slightly lower sensitivity and specificity when trainees performed PHHE compared with experts. Panoulas *et al.*<sup>19</sup> showed improved diagnostic accuracy when medical students and junior doctors added a PHHE examination to history, physical examination, and ECG findings. Our results are in line with their findings when PHHE is performed by non-experts. The feasibility is overall very good, 75–100% for all structures except the pulmonic valve and the abdominal aorta which were assessed to satisfaction in approximately one-half of the patients. Inexperienced users may be less able to provide optimal image quality and need better image quality to be able to interpret the recordings compared with expert users, but we have no data to support this hypothesis. The abdominal aorta was assessed in a relatively small number of patients compared with expert studies.<sup>7,20</sup> This may partly be explained by the fact that the residents did not register the aorta as assessed unless the entire length of the aorta was satisfactorily assessed. Secondly, patients were non-fasting, thereby reducing abdominal image quality, and BMI was  $\sim 2$  kg/m<sup>2</sup> higher in whom the abdominal aorta was not assessed ( $P < 0.001$ ). Nonetheless, there may have been too little focus on examining the great vessels during the training period.

The assessment of the global left-ventricular function and the pericardial and pleural space compared excellently with standard diagnostics. These are crucial issues in the cardiovascular ultrasound examination.<sup>21</sup> The classification/assessment of valvular function showed moderate-to-strong correlation and we found high specificity and high negative predictive values for detecting at least moderate valvular pathology. Importantly, no serious findings were missed, neither according to aortic valve pathology or regurgitation of the atrioventricular valves. However, there was



**Figure 4** Classification of ventricular and valvular pathology by PHHE compared with reference echocardiography. The agreement of PHHE and reference echocardiography in the quantification of ventricular and valvular pathology is illustrated. Over- and underestimation is the total numbers of misclassifications. In total, only 2% were misclassified by two degrees, the rest by one degree. LV, left ventricle; N, numbers; regurg, regurgitation.



**Figure 5** Cases illustrating the comparison of PHHE with reference method. (A) shows images from the pocket-size device, while (B) shows images from the high-end Vivid 7 scanner (GE Vingmed Ultrasound). 1 (A and B): 54-year-old man with principal diagnosis of liver cirrhosis changed to dilated cardiomyopathy after PHHE. 2 (A and B): 70-year-old man with known heart failure concluded to be decompensated after finding the shown significant amount of pleural effusion, dilated vena cava inferior, and reduced LV function. 3 (A and B): 75-year-old man referred with stroke where PHHE revealed an unknown moderate aortic regurgitation (without importance for the acute treatment). 4 (A and B): 88-year-old woman admitted with heart failure. PHHE revealed dilated ventricles, the shown large tricuspid regurgitation, pleural effusion, and ascites due to hypervolaemia.

some under- and overestimation of both ventricular dysfunction and valvular pathology. This may be explained by less experienced users, a very sensitive colour mode, and the lack of spectral Doppler in the PHHE devices. We find the presented degree of misclassification of aortic stenosis, in line with the presented, but less pronounced overestimation of aortic stenosis related to the lack of spectral Doppler in recent studies.<sup>6,7</sup> No moderate or severe aortic stenosis was missed. Atrioventricular valves regurgitations were missed more often compared with aortic regurgitations and this may be related to the higher number of atrioventricular regurgitations in the presented population. Due to moderate feasibility, the correlation of the aortic diameter was tested in only 52 patients and in these patients there was a strong agreement, and in the one misclassified, the difference was 4 mm. No aneurysms were missed by PHHE. The moderate agreement between PHHE and standard diagnostics in the assessment of the inferior vena cava may be explained by the period of time between PHHE and the standard echocardiography of median 21 h. Physiological variations and treatment effects may have influenced the results.<sup>22</sup> In addition, measurements of the size of the LA and vena cava inferior may be influenced by the fact that the pocket-size device lacks ECG-cables and there are limited opportunities to ensure the correct timing in the cardiac or respiratory cycles.

Taking a thorough medical history and performing a physical examination will remain the cornerstones in the diagnostic procedure, but there is a need for improvement in diagnostic accuracy to decrease medical errors.<sup>1,23</sup> PHHE is an excellent tool to provide further diagnostic information. As stated by the EACVI (former EAE) the users level of competence is very important in these devices.<sup>24</sup> Experienced ultrasonographers can start using PHHE without limitations. In less-experienced users, targeted education and a training period are necessary and PHHE should be used only for targeted examinations depending on the skills of the user.

Even in the hands of relatively inexperienced residents, PHHE provides feasible and reliable information at the point-of-care and improves the diagnostic precision without significant time delay. However, it is important to state that PHHE cannot replace the standard echocardiographic examination performed by experts in the echo lab. It should remain a bedside imaging tool which allows for quick and important information without losing valuable time.

## Limitations

In the study period, 1076 emergency admissions to the medical department were recorded and 84 of these patients declined consent. Out of the 446 patients randomized to receive PHHE examination, only 199 actually received it. This is mainly explained by busy working hours, hospital logistics, and the residents being informed to have a priority on standard diagnostics and treatment of patients.

The study was a single-centre study with a limited number of participating residents and patients. Consecutive patients were included and critical diagnosis such as aortic dissection and cardiac tamponade were not registered during the inclusion period. It is important to emphasize that in such cases, PHHE

may offer a fast track to the correct diagnosis,<sup>10</sup> but negative findings must not rule out further diagnostic tests if the clinician still suspects specific conditions.

## Conclusion

By adding a point-of-care PHHE examination lasting <6 min, medical residents were able to obtain reliable information of important cardiac structures and great vessels in patients admitted to a medical department. Thus, a focused examination with PHHE performed by residents, after a targeted training period have the potential to improve in-hospital diagnostics and care.

## Supplementary material

Supplementary material is available at *European Heart Journal – Cardiovascular Imaging* online.

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# Paper IV



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## Original article

## Routinely adding ultrasound examinations by pocket-sized ultrasound devices improves inpatient diagnostics in a medical department

Ole Christian Mjølstad<sup>a,b,\*</sup>, Havard Dalen<sup>a,c</sup>, Torbjorn Graven<sup>c</sup>, Jens Olaf Kleinau<sup>c</sup>,  
Oyvind Salvesen<sup>d</sup>, Bjorn Olav Haugen<sup>a,b</sup><sup>a</sup> MI Lab and Department of Circulation and Medical Imaging, Norwegian University of Science and Technology, Postboks 8905, 7491 Trondheim, Norway<sup>b</sup> Department of Cardiology, St. Olav, Trondheim University Hospital, Postboks 3250 Sluppen, 7006 Trondheim, Norway<sup>c</sup> Levanger Hospital, Nord-Trøndelag Health Trust, 7600 Levanger, Norway<sup>d</sup> Department of Cancer Research and Molecular Medicine, Norwegian University of Science and Technology, Postboks 8905, 7491 Trondheim, Norway

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## ABSTRACT

**Background:** We aimed to investigate the potential benefit of adding a routine cardiac and abdominal diagnostic examination by pocket-sized ultrasound device in patients admitted to a medical department.**Methods:** A random sample of 196 patients admitted to the medical department at a non-university hospital in Norway between March and September 2010 was studied. The patients underwent cardiac and abdominal screening with a pocket-sized ultrasound device with B-mode and color flow imaging after a principal diagnosis was set. Three internists/cardiologists experienced in ultrasonography performed the examinations. Diagnostic corrections were made and findings were confirmed by high-end echocardiography and examinations at the radiologic department.**Results:** 196 patients were included (male = 56.6%, mean  $\pm$  SD; 68.1  $\pm$  15.0 years old). The time spent doing the ultrasound screening was mean  $\pm$  SD 4.3  $\pm$  1.6 min for the cardiac screening and 2.5  $\pm$  1.1 min for the abdominal screening. In 36 (18.4%) patients this examination resulted in a major change in the primary diagnosis. In 38 (19.4%) patients the diagnosis was verified and in 18 (9.2%) patients an important additional diagnosis was made.**Conclusion:** By adding a pocket-sized ultrasound examination of <10 min to usual care, we corrected the diagnosis in almost 1 of 5 patients admitted to a medical department, resulting in a completely different treatment strategy without delay in many of the patients. Routinely adding a cardiac and abdominal ultrasound screening has the potential to rearrange inpatients workflow and diagnosis.

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## 1. Introduction

Despite the heavy arsenal of diagnostic modalities available in hospitals, autopsies have revealed major diagnostic errors on 30% of patients [1, 2]. Thus, there is a need for improvement in diagnostic accuracy. Ultrasonography performed bedside (point-of-care ultrasonography) by the clinician can rapidly provide diagnostic images as a supplement to clinical findings. This may decrease medical errors [3].

The last two decades have dramatically changed the quality and portability of ultrasound scanners [4–6]. In the hands of experts, echocardiography with hand-carried and the new pocket-sized ultrasound devices have been shown to be feasible and accurate [7–12]. Pocket-sized ultrasound devices fit in a white coat pocket, they are priced below \$10,000 and they can be operated easier than a standard

smart-phone. These devices may serve as efficient tools during busy ward rounds and thus, may provide a more efficient diagnostic algorithm and have the potential to rearrange inpatient workflow. However, clinical evaluation studies are scarce.

Thus, we aimed to study the diagnostic influence of focused cardiac and abdominal screening with pocket-sized ultrasound devices in an unselected group of patients admitted to a medical department.

## 2. Materials and methods

## 2.1. Study population

Patients admitted to the department of medicine at the non-university Levanger Hospital in Norway were screened with a pocket-sized ultrasound device. The department is sectioned into wards for cardiology, nephrology, gastroenterology, hematology and infectious diseases, pulmonary diseases, and geriatric and cerebrovascular diseases. The inclusion of patients was restricted to preset dates where one of three participating internists/cardiologists was the specialist

\* Corresponding author at: Mailing address: MI Lab and Department of Circulation and Medical Imaging, Norwegian University of Science and Technology, Postboks 8905, 7491 Trondheim, Norway. Tel.: +47 970 34 285; fax: +47 72 82 83 72.  
E-mail address: [ole.c.mjolstad@ntnu.no](mailto:ole.c.mjolstad@ntnu.no) (O.C. Mjølstad).

on call for general medicine. All three specialists have advanced competence level in echocardiography according to EAE recommendations [13]. They were also experienced with abdominal ultrasound, having performed more than 500 examinations each. The patients were included in the period from March 1st 2010 to September 30th 2010. The participating specialists performed 49 evening ward rounds in the study period. All patients admitted to the medical department on these dates and who were available for examination at the units before the evening ward round (5–7 pm) were included after written, informed consent was obtained.

Firstly, patients were admitted to the emergency room in a standard way and triaged according to their symptoms. Secondly, a resident or registrar carefully took a medical history and performed a physical examination (PE). Laboratory testing and diagnostic imaging was done in a normal goal-directed manner. Thus, usual care diagnostics were done prior to the screening with pocket-sized ultrasound device. No patient underwent high-end echocardiography or MRI prior to inclusion and only 5 were examined with CT scans or abdominal ultrasound at the radiologic department prior to inclusion.

## 2.2. Pocket-sized ultrasound screening

Cardiac and abdominal screening was performed with the pocket-sized ultrasound device (Vscan, GE Healthcare, Horten, Norway). This device offers B-mode and color flow imaging. A phased array probe with bandwidth of 1.7 to 3.8 MHz was used. This is a truly pocket-sized device with a total weight of 390 g (display-unit and probe) (Fig. 1).

The ultrasound screening was performed with the participants in left lateral decubitus position, as well as in back rest position for examination of abdominal organs and pleura. The cardiovascular screening included parasternal long- and short axis views and apical 4-chamber, 2-chamber and long axis views. All views were with gray scale and color Doppler recordings.

Right and left ventricular function was assessed semiquantitatively from the apical and parasternal recordings and classified as normal/near normal, moderate dysfunctional or severe dysfunctional. All four valves were examined from the standard views. Valvular pathology/dysfunction was classified semiquantitatively (mild, moderate or severe). Grading of stenosis was based on degree of calcification and movement of the leaflets, while grading of regurgitations was based on the color Doppler flow signal and size and function of the adjacent chambers. The left atrium was measured in end-systole on parasternal long axis recordings and classified as normal (<40 mm), moderately dilated (40–50 mm) and severely dilated (> 50 mm). The inferior vena



**Fig. 1.** Demonstration of the pocket-sized device Vscan. Illustration from MI Lab, Norwegian University of Science and Technology. Picture does not reflect the presented study.

cava was assessed at the ends of expiration and inspiration from the sub costal window to estimate right atrial pressure [14]. Both pleural cavities were examined with patient in supine position and if pleural effusion was present, the amount was graded as significant or non-significant amount of effusion. A significant amount of effusion was graded if the diameter of fluid between the thoracic wall and the lung exceeded 5 and 4.5 cm in the left or the right pleural cavity. By the abdominal ultrasound screening the gallbladder and liver were classified as normal or abnormal, where ultrasound evidence of cholecystitis, cholelithiasis or intrahepatic tumors are examples of abnormal findings. The kidneys were classified as normal, evidence of hydronephrosis or other pathology. The abdominal aorta was assessed from the diaphragm to the bifurcation.

Diagnostic corrections were made after the pocket-sized ultrasound screening. All diagnostic changes were confirmed by standard diagnostic procedures, i.e. a complete echocardiographic examination, abdominal ultrasound, CT or MRI scanning according to the medical condition suspected. In addition, all patients admitted to the cardiac unit were routinely planned for high-end echocardiography regardless of the findings by pocket-sized ultrasound screening. All the clinicians who performed the pocket-sized ultrasound examinations had access to clinical information including the preliminary diagnosis. However, the radiologist and cardiologist who performed the high-end reference imaging procedures were blinded to the result of the pocket-sized ultrasound examination.

## 2.3. Clinical usefulness of the routinely added ultrasound examination

All patients were discussed in an end-point committee consisting of two residential and one external (St. Olav, Trondheim University Hospital) internists/cardiologists experienced in echocardiography and abdominal ultrasonography. The committee members made separate decisions based on medical journals and diagnostic tests blinded to the decisions of the other members, and graded the diagnostic usefulness of the bedside pocket-sized ultrasound screening into one of the following categories: 1) The principal diagnosis was changed, 2) the principal diagnosis was confirmed, 3) an additional diagnosis important for in hospital or post discharge follow-up, which did not influence the treatment of the principal diagnosis, was made or 4) the results from the screening with pocket-sized device did not have any impact on the actual stay or the follow up of the patient. In case of disagreement the majority of the committee had the preference.

## 2.4. Statistical analysis

As the different echocardiographic and anthropometric measures partly departed from normal distribution the basic characteristics are presented as mean  $\pm$  standard deviation (SD) and range. Comparison of continuous variables between groups was analyzed using the non-parametric Mann–Whitney *U* Test of independent samples, and comparison of proportions between groups was analyzed using the Chi square test or Fisher's exact test. Spearman's rho (*r*) was used for comparison of the ranking of pathology between the pocket-sized and the high-end echocardiographic or radiologic examinations. Data are presented as *r* (95% confidence interval (CI)) with the 95% CI computed using bootstrapping. For comparison of continuous variables between the pocket-sized and the high-end examinations Pearson's rho (*r*) was used. In logistic regression analyses predictors for diagnostic usefulness of the additional ultrasound examination were studied. Change of primary diagnosis or any diagnostic usefulness assessed (change or verification of primary diagnosis, or an important additional diagnosis) was used as dependent variable, and age and risk factors were included as independent variables. In these analyses age was entered as a continuous variable. Statistical analyses were performed using SPSS for Windows version 18.0 (SPSS, Inc., Chicago, IL).

2.5. Ethics

The study was approved by the Regional Committee for Medical Research Ethics, and conducted according to the Helsinki Declaration. All the patients gave their informed consent to participate in the study.

3. Results

Table 1 shows the baseline data of the 196 patients included in the study (111 men and 85 women). Mean ± SD (range) age was 68.1 ± 15.0 (20–95) years. The distribution of age was positively skewed compared to a normal distribution. Atrial fibrillation was present in 32 (16%) of the patients at admission, hypertension was present in 69 (35%) patients and 32 (16%) had known diabetes mellitus. Cardiovascular disease defined as at least one of the following diagnoses; myocardial infarction, angina pectoris, heart failure, cerebrovascular disease or peripheral vascular disease was present in 91 (46%) patients. Malignant disease was prior diagnosed in 16 (8%) patients.

3.1. Pocket-sized ultrasound screening

The abdominal aorta was completely assessed in 142 (72%) participants. The inferior vena cava was assessed in 164 (84%) and the gallbladder was visualized in 154 (78%). Left and right ventricular function indices were assessed in at least 194 (99%), all other described structures were assessed to satisfaction in at least 187 (95%) participants [15]. The total time used for the ultrasound examinations was 6.8 ± 2.0 min: 4.3 ± 1.6 min for the cardiovascular screening and 2.5 ± 1.0 min for the focused abdominal screening.

3.2. Clinical usefulness

The diagnostic usefulness of bedside cardiovascular and abdominal ultrasound screening with the pocket-sized ultrasound device is shown in Table 2. In total 36 (18%) participants had the main diagnosis changed after the pocket-sized ultrasound examination compared to the principal diagnosis based on usual care diagnostics. Table 3 shows baseline characteristics, the preliminary diagnosis, diagnostics included in the preliminary diagnosis, findings by pocket-sized ultrasound, the new diagnosis and therapeutic implications for these patients. The principal diagnosis was verified in 38 (19%) patients. An additional important diagnosis without influence on the current stay was made in 18 (9%) patients. In 104 (53%) patients the pocket-sized screening did not have any impact on the actual stay or the follow up of the patients.

**Table 1**  
Basic characteristics of the study participants.

	Mean ± SD*
Age, years, mean ± SD (range)	68.1 ± 15.0 (20–95)
Women, N (%)	85 (56.6)
Height, cm	171.7 ± 9.5
Body mass index, kg/m <sup>2</sup>	26.9 ± 5.8
Systolic blood pressure, mm Hg	144.6 ± 31.3
Diastolic blood pressure, mm Hg	78.7 ± 18.6
Heart rate, bpm	80.5 ± 21.6
Atrial fibrillation, N (%)	32 (16.3)
Known hypertension, N (%)	69 (35.2)
Known diabetes, N (%)	32 (16.3)
Known myocardial infarction, N (%)	47 (24.0)
Known angina, N (%)	36 (18.4)
Known heart failure, N (%)	17 (8.7)
Known peripheral vessel disease, N (%)	18 (9.2)
Known stroke, N (%)	26 (13.3)
Known cardiovascular disease, N (%)	91 (46.4)
Known cancer, N (%)	16 (8.2)

\* Data are mean ± SD unless specified.

**Table 2**  
Diagnostic usefulness of bedside cardiovascular and abdominal ultrasound screening with the pocket-sized ultrasound device.

	Number (%)
Change of primary diagnosis	36 (18.4%)
Verification of primary diagnosis	38 (19.4%)
Additional diagnosis made	18 (9.2%)
No diagnostic usefulness	104 (53.1%)

Among the 36 patients with change of preliminary diagnosis, all three members of the end-point committee completely agreed in 33 (92%) patients and disagreed in the last 3 cases. In the latter three cases the minority of the committee voted for “diagnosis verified” and the majority voted for “diagnosis changed”. None of those who had the diagnosis changed following pocket-sized ultrasound had this diagnosis changed thereafter.

3.3. Feasibility and accuracy

The correlation of pocket-sized echocardiography and high-end echocardiography was  $r \geq 0.85$  for grading the left ventricular regional function, left and right ventricular global function, valvular function, pleural- or pericardial effusion and detection of abdominal aortic aneurysms. Left atrial size and inferior Vena cava dimensions showed correlations of  $r$  (95% CI) 0.65 (0.51–0.77) and 0.68 (0.53–0.80). Assessment of pathology in liver/gallbladder and kidneys showed kappa values of (95% CI) 0.90 (0.75–1.0) and 0.83 (0.68–0.96), respectively.

Sensitivity and specificity of pocket-sized ultrasound screening with respect to detect at least moderate dilatation of left atrium was 0.81 and 0.68. The sensitivity/specificity with respect to detect at least moderate LV dysfunction, any regional LV dysfunction and any RV dilatation or dysfunction was 0.97/0.99, 0.97/0.99 and 0.90/0.99. All other described cardiac indices showed sensitivity and specificity  $\geq 0.89$ . Correspondingly, the sensitivity/specificity with respect to detect any abdominal aortic aneurysm ( $> 35$  mm), any pathology in the kidneys or liver/gallbladder was 0.89/1.0, 0.94/0.98 and 0.93/0.97.

3.4. Predictors of usefulness

When evaluating predictors of diagnostic usefulness, the odds ratio (OR) (95% CI) for any diagnostic usefulness (defined as the above categories 1, 2 and 3) was 1.6 (1.3–2.0) per 10 years higher age ( $p < 0.001$ ) and 2.0 (1.7–2.3), ( $p = 0.02$ ) for those with known cardiovascular disease (CD). In the group of patients with either established cardiovascular disease or increased risk of CD (hypertension, diabetes mellitus) the odds ratio (95% CI) was 2.9 (2.6–3.2), ( $p < 0.001$ ). Correspondingly, data for change of the primary diagnosis was 1.6 (1.4–1.9), per 10 years higher age ( $p = 0.003$ ) and 1.2 (0.8–1.6) for those with known CD ( $p = 0.6$ ). In the group of patients with either known CD or increased risk the OR (95% CI) was 3.0 (2.5–3.4), ( $p = 0.02$ ). Figs. 2 and 3 show how age influenced the usefulness of the screening examination.

4. Discussion

By routinely adding a cardiac and focused abdominal ultrasound screening to the standard diagnostic examinations performed in the emergency room, the principal diagnosis, and thereby the treatment, was significantly corrected in nearly 1 in 5 (18%) of patients. Additionally, 20% had their primary diagnosis verified and in 9% an additional diagnosis of certain importance was made. Overall, the pocket-sized ultrasound screening of mean 6.8 min was of diagnostic importance in approximately half of all patients.

The population was randomly selected on the basis of preset days when the participating physicians were on call and therefore

**Table 3**  
Baseline characteristics, diagnostic tests, ultrasound findings and therapeutic implications in the 36 participants with change of primary diagnosis.

Baseline characteristics	Medical unit	Preliminary diagnosis	Diagnostics included in preliminary diagnosis	Findings by pocket-sized US	New diagnosis	Therapeutic implications
M75y, HT, MI	Cardiac	Rehab. after CABG	ECG; normal, CXR; unilateral small amount of pleural effusion, lab; Hb 9.3 g/dl, CRP 217 mg/l	AAA 56 mm, pericardial and pleural effusion	AAA. Postpericardiotomy syndrome	Diuretics†. Referral to vascular surgery
M73y, HT, AP, DM, PVD, CVD, T <sub>4</sub> ↓	Gastroenterology	Oesophagitis	ECG; normal, CXR; normal, lab; Hb 10 g/dl	Anteroapical hypokinesia	Myocardial infarction	Transfer to coronary unit. Anticoagulation and platelet inhibition. Referral for coronary catheterization
F82y, HT, AP, bAVR	Cardiac	Rehab. after CABG	ECG; normal, CXR; small amount of pleural effusion, lab; normal	Pleural effusion, significant amount	Post-CABG with pleural effusion	Increased diuretics
F78y, asthma	Cardiac	ACS	ECG; normal, CXR; normal, lab; normal	Normal LV. Moderate aortic stenosis.	Aortic stenosis	Follow up due to aortic stenosis
F82y	Cardiac	Angina	ECG; non-specific ST-T changes, CXR; normal, lab; non-specific liver enzymes elevation	Cholelithiasis, gallbladder wall thickening and double wall sign	Cholecystitis	Immediate transfer to surgical department. Treated with antibiotics.
M90y, HT, pacemaker	Cardiac	Heart failure	ECG; Paced rhythm, CXR; Unilateral pleural effusion, lab; creatinine 157 µmol/l (unchanged), Tnl 110 ng/l.	Biventricular failure. Severe urinary retention. Severe hydronephrosis	Hydronephrosis. Urinary retention	Catheterization of urinary bladder (4.5 L). Antibiotics. Secondly treatment for heart failure.
M89y, HT, AP, PVD (2004; AAA op.)	Pulmonary	Pneumonia?	ECG; normal, RBBB, CXR; basal atelectasis, lab; CRP 51 mg/l	AAA 53 mm.	AAA	Patient transferred to nursing home. No implications.
M83y, HT, AP, PVD, AAA, CKD	Nephrology	Generalized malaise	ECG; AFL 4:1. CXR; Some PIE, infiltration left side. CT thor./abd; AAA, lab; creatinine 628 µmol/l, Hb 10.8 g/dl	Reduced LV function, pleural effusion, VCI 25/25 mm. (AAA)	Heart failure. CKD.	Given high doses of diuretics. (patient refused to start dialyses)
F83y, HT, COPD, pacemaker	Pulmonary	COPD	ECG; AFIB 120/min, lab; Tnl <20 ng/l, CRP 42 mg/l, CXR; Bilateral lung infiltrate	Severe LA dilatation, reduced LV long-axis function. PIE. Moderately dilated RV	Diastolic heart failure. AFIB	Diuretics. Non-invasive ventilatory support.
M80y, HT	Pulmonary	Pneumonia	ECG; sinus, LBBB, CXR; Lung infiltrate. PIE, lab; CRP 52 mg/l.	Multiple hepatic lesions, hydronephrosis, PIE	Metastatic (urinary bladder) cancer	Transfer to surgical department. Metastatic urinary bladder cancer verified. Operated. Rehydration
F77y, AP, HF, PVD, CKD, COPD, AAA	Nephrology	Diverticulitis	ECG; normal, CXR; normal, abd. US; AAA, small kidneys, lab; creatinine 456 µmol/l, sodium 135 mmol/l, potassium 4.5 mmol/l, CRP 96 mg/l	Hypovolaemia (VCI slim, high collapsibility), AAA 40 mm, small kidneys, serious LV hypertrophy.	Hypovolaemia	
M70y, MI, pulmonic ca.	Pulmonary	Generalized malaise/ pulmonic ca.	CXR; normal (no tumor visualized), lab; liver enzymes elevated, Hb 10.8 g/dl,	Liver lesions, dilated bile ducts, pericardial effusion	Liver metastasis. Cholestasis	Immediate ERCP. Biliary sphincterotomy and stent.
M75y, AP, PVD, pulmonic ca.	Cardiac	Heart failure	ECG; AFIB, 105/min, no ischemia, CXR; infiltration and tumor right lung, lab; normal	Normal echocardiography and abdominal US.	COPD. Respiratory regurgitation	Heart failure ruled out. Dyspnoea related to respiratory regurgitation. Referral for spirometry. Treated with steroids.
F60y, HT, T <sub>4</sub> ↓	Cardiac	ACS?	ECG; Sinus, T-wave inv., left axis, CXR; normal; lab; Tnl 45 ng/l.	Concentric LV hypertrophy	Hypertensive heart disease	Antihypertensive treatment optimized. SPECT; no reversibility
F76y, osteoporosis	Nephrology	Hyponatraemia	ECG; sinus, T-wave inv., CXR; normal, lab; sodium 116 mmol/l, potassium 2.8 mmol/l, creatinine 40 µmol/l	Severe mitral regurgitation	Prolapse of the mitral valve. Mitral regurgitation	Referral for surgery. Operated.
F66y, HT	Cardiac	ACS	ECG; sinus, left axis dev.	Dissection of the ascending aorta, secondary aortic regurgitation	Aortic dissection	Immediate transfer for surgery. Operated.
F92y, HT	Pulmonary	Pulmonary embolism?	ECG; normal, CXR; infiltration right lung, lab; normal	Dilated LV, globally reduced LV function, hypervolaemia (dilated IVC, pleural effusion)	Heart failure	Diuretics
F59y, HT, MI	Cardiac	ACS	ECG; First degree AV block I, CXR; normal	Dilated LV, reduced LV systolic function, severe aortic regurgitation	Aortic regurgitation. Operated.	Heart failure treatment. Referral for valvular surgery. Operated.
M70y	Cardiac	AFL	ECG; AFL, T-wave inv., CXR; normal	Severe apical hypokinesia, EF 30%	Myocardial infarction	Transfer for coronary catheterization.
M33y, Crohn's disease	Gastroenterology	Crohn's disease	Lab; sodium 139 mmol/l, potassium 3.4 mmol/l, creatinine 90 µmol/l, CXR; normal	Hypovolaemia (IVC slim, max 8 mm, high collapsibility).	Dehydration.	Immediate rehydration (6000 ml iv. in 24 h)
F58y, HT	Cardiac	Non-specific chest pain	ECG; left axis, non-specific ST-T changes, lab; normal (Tnl↑ shown later)	Regional anterior hypokinesia, EF 50%	NSTEMI	Transfer for coronary catheterization. CABG.
F80y, AFIB, MI, HF, CVD	Cardiac	Pneumonia	ECG; AFIB, 82/min, CXR; Mild deterioration – infectious? Congestion?	Reduced LV function, anterior scar, EF 30%.	Heart failure, post MI	Diuretics. Heart failure treatment.

Table 3 (continued)

Baseline characteristics	Medical unit	Preliminary diagnosis	Diagnostics included in preliminary diagnosis	Findings by pocket-sized US	New diagnosis	Therapeutic implications
M80y, MI, pulmonic ca.	Nephrology	Generalized malaise	CXR; minor pleural effusion, lab; CRP 109 mg/l, liver enzymes; normal	Liver lesions, pericardial effusion	Metastatic pulmonic ca.	Palliative treatment
M88y, MI, PVD, prostatic ca.	Stroke	Confusion, stroke?	ECC; sinus, LBBB, CXR; left pulmonary infiltrate, CT cerebral; normal	Akinisia anterior wall, EF 20%, elevated LA filling pressures (stiff LV, dilated LA)	Heart failure, post MI	Diuretics. Heart failure treatment.
F67y, HT, DM, PVD	Cardiac	AFIB	ECC; AFIB, 140/min, CXR; Mild congestion	Near normal LV, dilated LA, hypervolaemia (pleural effusion, dilated IVC)	Diastolic heart failure. AFIB	Diuretics, salt restriction, frequency optimization
M62y, MI, DM	Cardiac	Pneumonia	ECC; Paced rhythm, 60/min, CXR; Infiltrate? Congestion?, lab; creatinine 192 µmol/l, Tnl 156 ng/l	Severe mitral regurgitation reduced LV function, EF 35%	Mitral regurgitation. Heart failure	Increased diuretics. Referral for follow-up due to mitral regurgitation other region.
F82y, HT, PVD, CVD	Cardiac	ACS?	ECC; normal, CXR; no congestion, lab; potassium 3.2 mmol/l	Hypervolaemia (dilated IVC), normal LV	Hypervolaemia.	Diuretics/spironolactone
F82y, HT, recent op. (hip fracture)	Cardiac	Pneumonia. Heart failure.	ECC; sinus tachycardia, 104/min, CXR; basal right pulmonary infiltrate, lab; INR 2.5, CRP 45 mg/l	Severe dilation of RV. Septal flattening in diastole. Moderate tricuspid regurgitation. IVC dilated no collapsibility.	Pulmonary embolism	Optimization of anticoagulation. CT scan verifies pulmonary embolism.
M53y, asthma	Cardiac	ACS?	ECC; Poor R-wave progression, CXR; mild congestion or infiltrate right lung	Dilated LV, reduced LV function, EF 25%	Dilated cardiomyopathy	Treatment for heart failure, MRI verifies DCM
F56y, asthma	Cardiac	Pulmonary embolism?	ECC; normal, CXR; no congestion, lab; D-dimer 2.7 mg/l, CRP <5 mg/l, (Tnl† shown later)	Hypokinesia inferior wall. Normal RV	NSTEMI	Referral for fast coronary catheterization
F88y, AFIB, HT	Stroke	Stroke? Herpes zoster	ECC; AFIB, 130/min, lab; CRP 27 mg/l, CXR; normal, CT cerebral; normal	Moderate pericardial effusion	Metastatic (pulmonic) cancer	Referral for thoracic CT that revealed metastatic pulmonic ca.
M89y, AFIB, MI, AP, HF	Cardiac	Heart failure?	ECC; AFIB 86/min, CXR; no congestion, mildly enlarged heart, lab; Tnl 150 ng/l	Severe aortic stenosis, reduced LV function	Aortic stenosis. Heart failure	Diuretics. Transfer to nursing home.
F78y, HT, DM	Nephrology	Generalized malaise	ECC; normal, CXR; normal, lab; creatinine 73 µmol/l, sodium 141 mmol/l, potassium 4.0 mmol/l	Hypovolaemia (slim IVC <5 mm, high collapsibility)	Hypovolaemia	Rehydration (2000 ml iv. in 4 h)
M86y, HT, CVD	Nephrology	Stroke?	ECC; normal, CXR; normal, CT cerebral; normal, lab; Tnl 120 ng/l, CRP 174 mg/l, PSA 125 µg/l	Urinary retention, hydronephrosis, urinary bladder tumor, cholelithiasis	Urinary bladder cancer	Investigation revealed prostatic ca. Medical treatment (antiandrogens and GnRH agonists).
F81y, MI	Cardiac	Syncope	ECC; sinus, AV block I, CXR; normal, CT cerebral; normal, lab; D-dimer >7.2 mg/l	AAA; 10 cm	AAA	Referral for surgery. Operated.
M83y, HT, MI, AP, COPD	Pulmonary	COPD	ECC; AFIB, 67/min, CXR; non-specific atelectasis, lab; D-dimer 0.9 mg/l, CRP <5 mg/l	Dilatation and hypertrophy of RV, diastolic septal flattening	Cor pulmonale	Optimization of medical treatment (contraindications for anticoagulation therapy)

Abbreviations: AAA; abdominal aortic aneurysm, abd; abdominal, AFIB; atrial fibrillation, AFL; atrial flutter, AP; angina, AV; atrioventricular, bAVR; aortic valve replacement (biologic), ca; cancer, CABG; coronary artery bypass graft, CXR; chest X-ray, CKD; chronic kidney disease, COPD; chronic obstructive pulmonary disease, CRP; C-reactive protein, CVD; cerebrovascular disease, DCM; dilated cardiomyopathy, DM; diabetes mellitus, ECC; electrocardiogram, ERCP; Endoscopic retrograde cholangiopancreatography, GnRH; gonadotropin-releasing hormone, Hb; hemoglobin, HF; heart failure, HT; hypertension, iv; intravenous, IVC; inferior vena cava, inv; inversions, LBBB; left bundle branch block, LV; left ventricular, MI; myocardial infarction, NSTEMI; non ST-elevation myocardial infarction, op.; recent surgery, PIE; pleural effusion, T<sub>4</sub>; Hypothyroidism, PSA; prostate-specific antigen, PVD; peripheral vascular disease, Tnl; Troponin I, thor; thoracic, US; ultrasound.

represents an unselected population in our department. The distribution of age was positively skewed and the baseline characteristics were in line with prior studies suggesting that the population reflects the everyday patients admitted to a general medical department [16–19].

In line with former studies we showed that in the hands of experts the pocket-sized scanners are feasible and offer highly accurate assessment of cardiac structures and the abdominal large vessels [8, 10–12, 20]. It is important to emphasize that a pocket-sized scanning does not replace a standard echocardiographic examination. However, as shown by the good correlation between pocket-sized ultrasound and high-end echocardiography pocket-sized ultrasound devices may work as an excellent screening tool as well as a tool in selecting the right patients for the high-end echocardiography [15, 21, 22]. Most importantly, these scanners are quick and easy to use and our study shows their ability to improve the diagnostic precision.

Previous studies have shown prevalent findings of abdominal aortic aneurysms (AAA) and reduced left ventricular ejection fraction in high-risk populations [23, 24]. In a hypertensive population 6.5% of the

patients had AAA [24]. Baker et al. screened patients with previous myocardial infarction and found that 15.4% had left ventricular ejection fraction <45% [23]. An argument against screening may be incidental findings (IF). Among emergency admissions Soultati et al. found that 28.2% had IF, especially in abdominal organs and in older patients. However, 21% of the IF were clinically significant and in need of further management [25]. Our study showed the highest diagnostic usefulness in the elderly population and in the population with, or in high risk of developing, cardiovascular disease.

As shown previously it is challenging to make a correct diagnosis based on medical history, physical examination and goal-directed laboratory tests and imaging procedures. A missed or delayed diagnosis may in worst-case scenario be lethal [1, 2]. Modern medicine has brought us several tools offering more diagnostic confidence. However, most often these methods are associated with some time delay and in addition, computer tomography and X-ray are encumbered with ionization and magnetic resonance imaging has limited availability and significant contraindications. Point-of-care ultrasonography is defined as ultrasonography brought to the patient and performed by the

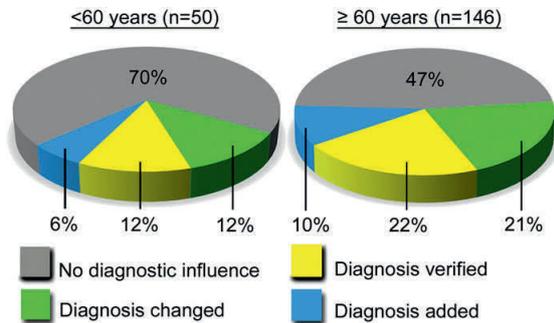


Fig. 2. Figure shows the increased diagnostic usefulness of routinely adding cardiovascular and focused abdominal ultrasound screening among those at older age. The oldest age group is shown to the right.

provider in real time [3]. In some of the presented patients we showed that this diagnostic modality represents the crucial step in making life-threatening diagnosis without delay.

The recently published statement from the European Association of Echocardiography (EAE) regarding with the use of pocket-size imaging devices states that pocket-size devices may serve as a complement to the physical examination and a tool for a fast initial screening in the emergency setting [26]. This statement is fully supported by our study that emphasizes the need of point-of-care diagnostics that improves primary diagnostics and inpatient care.

#### 4.1. Limitations

In our hospital the stay in the emergency room (ER) is mostly limited to the period of triaging, taking a medical history, performing a physical examination and starting immediate therapy. Routine diagnostics like arterial/venous blood samples and ECG are also performed, but very few imaging procedures other than standard chest X-rays are performed prior to admission to the medical department. Thus, the number of imaging procedures performed before admittance to the medical department may be lower compared to some hospitals.

Another limitation of this study is that the pocket-sized ultrasound screening was performed by internists experienced in both cardiovascular and abdominal ultrasound. All three internists were

also board certified cardiologists. The more realistic setting will probably be the examination performed in the emergency room by a resident or registrar with a limited education in diagnostic sonography. The EAE statements highlight the importance of these physicians going through a dedicated training program with the emphasis on cardiac physiology and pathology [26]. How our findings correspond to non-experts users is not known, but former studies have shown somewhat lower sensitivity and specificity [22, 27, 28]. In spite of this the ultrasound examinations may still be of significant value in high-risk populations. This has to be proven in further studies. We suggest that implementing strategies and systems for routinely adding a pocket-sized ultrasound examination to patients in medical departments are appropriate, but further studies must demonstrate the degree of education and training needed for the medical professionals performing these examinations.

Negative findings by abdominal ultrasonography were not systematically verified with other imaging modalities, but as shown, most cardiac and abdominal structures were assessed with high accuracy.

#### 5. Conclusion

By adding a pocket-sized ultrasound examination with B-mode and color flow imaging of <10 min to usual care diagnostics, we made important diagnostic changes in 1 of 5 patients admitted to a medical department, resulting in a completely different treatment strategy without time delay. Routinely adding a cardiac and abdominal ultrasound screening has the potential to rearrange inpatient workflow and diagnosis.

#### Learning points

- Despite a wide array of diagnostic modalities, clinical diagnostics are still sub-optimal and autopsy studies have revealed major diagnostic errors in a significant amount of patients treated at hospital.
- Point-of-care ultrasound performed by clinicians may be a useful supplement in the treatment and assessment of certain patients.
- By adding a cardiovascular and focused abdominal ultrasound examination of mean 6.8 min by pocket-sized ultrasound, we correctly assessed cardiac and abdominal structures' size and function enabling correction of the diagnosis in nearly 1 of 5 patients admitted to a general medical department.
- Additionally, closer to 30% of patients had their diagnosis verified or received an additional diagnosis important for treatment or follow-up made.

#### Conflict of interest

None declared.

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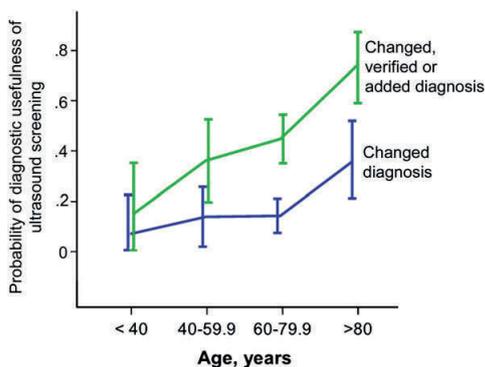


Fig. 3. Diagnostic usefulness of pocket-sized ultrasound examination according to age. Blue line refers to the probability of change of primary diagnosis following routinely added ultrasound examination. Green line refers to any diagnostic change classified as change of primary diagnosis, verification of primary diagnosis or adding another important diagnosis. Error bars reflect 95% confidence interval for the specified age groups.

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