Master's Degree course in Biomedical Engineering

Academic Year 2020/2021

Master's Degree Thesis

CMUT-BASED, PORTABLE, HANDHELD DEVICE ANALYSIS FOR DIAGNOSTIC ULTRASOUND IMAGING

Advisor
Prof. Eros Gian Alessandro Pasero
Co-Advisor
Ing. Annunziata Paviglianiti

Candidate
Chiara D'Elia

October 2021

Abstract

Diagnostic ultrasound is a non-invasive imaging modality that uses high-frequency sound waves to generate images of structures inside the body. Through the advancements of biomedical technologies, medical ultrasound systems have evolved and, especially in the last two decades, the miniaturization of ultrasound machines has become feasible. The advent of portable machines and the subsequent development of handheld devices have made possible an evolution for the role of ultrasounds in healthcare system, emerging as an invaluable tool for immediate first-level diagnosis wherever the patient is being treated, whether that's at emergency wards, at home, or in an ambulance. This practice is called point-of-care ultrasound (POCUS), and allows physicians to obtain immediate and quick assessments while evaluating their patients, as an aide to traditional examination techniques.

The purpose of this thesis is the study of a new pocket-sized ultrasound system, Butterfly iQ+, developed by the American company Butterfly Network. This device is composed by a single probe that is connected to a smartphone or tablet to display and record real-time ultrasound images. The very innovative aspect is the technology behind the Butterfly iQ+: traditional ultrasound machines commonly use piezoelectric crystal-based transducers, which convert electrical energy into mechanical energy in the form of ultrasound waves, and vice versa. This traditional technology is very expensive and requires the use of multiple probes. Therefore, Butterfly iQ+ has introduced an innovative way to send and receive ultrasound waves: it attempts to do the same work of piezoelectric ceramics by replacing them with a single silicon chip containing 9000 Capacitive Micromachined Ultrasound Transducers (CMUTs), which act like little drums to generate vibrations. This is called *Ultrasound-on-chip* technology and since it is based on semiconductor wafers industry, it allows to drastically reduce the device's costs. Moreover, unlike traditional piezoelectric crystals that are tuned to produce ultrasound waves at particular frequencies and image at defined depths, CMUTs provide a wider bandwidth, allowing the possibility to exploit a single probe for emulating any type of probes. As a result, the only ultrasound probe from the Butterfly iQ+ system can be used for multiple applications and can be programmed to image the whole body.

After analyzing the clinical and technical features, the pros and cons, and the innovative technology behind this new device, the thesis focuses on the image quality assessment in images acquired by Butterfly iQ+ system, as a tool to quantitatively evaluate the machine's performances. A series of parameters related to image quality in ultrasound have been measured and evaluated, and also compared to the same parameters obtained by images acquired with a traditional ultrasound machine. Moreover, a qualitative evaluation of Butterfly iQ+ images has been conducted in the clinical field. Finally, future applications for Butterfly iQ+ will be discussed.

Contents

List of figures

List of tables

Chapter 1

Introduction

1.1 A new generation of ultrasound: introducing Butterfly iQ+ device

The pocket-sized ultrasound tool studied in this thesis is Butterfly iQ+ device, a product of Butterfly Network (Butterfly Network, Inc, Guildford, CT, USA), an American company founded in 2011 by the scientist and entrepreneur Johnathan Rothberg. Rothberg was previously known for his ambitious efforts in next-generation DNA sequencing. His contribution in this field is particularly remarkable for the development of an integrated circuit realized with semiconductor manufacturing techniques able to perform DNA sequencing of genomes [1]. Since then, he always exploited the semiconductor-based technology, with the advantage of providing even more compact and low-cost solutions, for focusing on healthcare field, in particular on ultrasound. With the launch of Butterfly iQ (subsequently updated with the new release Butterfly iQ+) he revolutionized the fundamental physics of ultrasound, realizing a handheld ultrasound device whose core technology is a silicon chip, which replaces expensive piezoelectric materials used in transducers of all current commercially available ultrasound machines. In 2017, Butterfly Network announced its FDA 510(k) clearance for Butterfly iQ for 13 different clinical applications [2], while in 2019 it received CE Mark [3] and was classified as Class IIa portable ultrasound system [4], making it available for licensed healthcare professionals outside of the US.

Figure 1.1. Butterfly iQ+ system connected to a compatible mobile device [5].

The device itself is shown in figure 1.1. It consists in a pocket-sized single probe that works directly connecting to a compatible smartphone or tablet (Apple or Android mobile device) through either a Lightning or USB-C connector. Ultrasound scans performed by Butterfly probe are visible and recordable in real-time on the mobile device by using a dedicated Butterfly iQ App, which can be downloaded for free. The device can be charged wirelessly by means of a battery charger supplied with the probe; once fully recharged, it ensures 2 hours of continuous scan time.

1.2 CMUT technology behind Butterfly iQ+

Conventional ultrasound machines exploit the piezoelectric effect to transmit and detect ultrasound waves to produce an image. The application of an electric field induces piezoelectric materials (crystals or ceramics) to vibrate, resulting in the emission of acoustic waves travelling into the body until they hit an interface between different tissues. The larger is the difference in acoustic impedance between the tissues in the boundary, the greater will be the amplitude of the ultrasound wave reflected. Acoustic impedance is a physical property of tissues and it represents how much opposition is offered by the tissue in which the acoustic wave travels; it depends on the speed of the ultrasound wave and on the medium density. Piezoelectrics in transducers of common ultrasound systems also works in receiving mode: when they receive the reflected sound wave, in response to the consequent mechanical stress, they are able to generate an electric signal.

The limitations in this old technology using piezoelectric materials are represented by the excessive costs required for their production and use, and by the fact that piezoelectric transducers are by nature highly tuned devices: only at their specific resonant frequency they produce high-amplitude oscillations even with little forcing, while they barely move at other excitation frequencies [6]. This implies the necessary use of multiple probes to produce ultrasound waves at defined frequencies and create images at certain depths according to different applications. The three most used ultrasound probes used in standard ultrasound machines are:

- Linear array: piezoelectric crystals are positioned in a linear arrangement, creating a rectangular ultrasound beam with high operating frequencies. It is great for precise imaging at superficial examinations.
- Convex array: crystals are arranged in a curvilinear fashion and produce a fan shape. It's used to acquire images of deeper structures at the cost of the resolution, with lower operating frequencies.
- Phased array: used in case of targets placed behind objects that represent obstacles for ultrasounds, like bones, so the piezoelectric elements operate sequentially in phases to steer the ultrasound beam and allow the examination of transthoracic and transcranial structures. The ultrasound image produced has a cone shape.

With its innovative silicon-based technology, Butterfly iQ+ differentiates itself from all traditional ultrasound systems. As already mentioned, the use of semiconductor-based technology has made this ultrasound device much more accessible in terms of costs than all its preceding machines. The company leverages on an inexpensive, high-performance supply chain that is already in place, since it has revolutionized the consumer electronics industry, to take advantage and create its own way to generate and receive ultrasound waves. With *Ultrasound-on-chip*, this is how the new technology is called, the same chips used to produce various types of microelectromechanical systems, or MEMS, found in computers, phones, digital cameras, etc., are now used to replace traditional piezoelectric based-transducers. Chips are made starting from a semiconductor disc, a silicon wafer, that is realized by applying micromachining and MEMS fabrication techniques and is then diced into tens of little rectangular chips; each of them will be part of one ultrasound device. Each silicon chip contains a 2D array of over 9000 micromachines (as illustrated in figure 1.2) used as transducers, that act like little drums on it and wobble to generate vibrations.

Figure 1.2. Below the surface of Butterfly iQ+ [7].

These transducers are called Capacitive Micro-machined Ultrasound Transducers (CMUTs). A single CMUT basic structure is a capacitor cell formed by a top electrode consisting in a thin conductive membrane, that is suspended over a vacuum gap, and an underlying conductive substrate that acts as the bottom electrode. Driving the capacitors with an alternating voltage, the membrane is repeatedly first attracted toward the substrate by the electrostatic force, and then induced to resist to the attraction because of the mechanical restoring force due to its stiffness. This continuous process generates ultrasound vibrations that are transmitted into the body. On the contrary, when the membrane receives the ultrasound wave reflected from tissues, a constant bias voltage with a capacitance change is registered, and electrical current is consequently generated, allowing for the creation of the ultrasound image [8]. Therefore, even capacitive transducers are able to both generate and receive ultrasound waves.

Nevertheless, unlike piezoelectric transducers that are highly tuned devices, CMUTs can be tuned on the fly [9], because the great number of micromachine transducers contained in a single probe provides a huge dynamic range. A CMUT has its own resonant frequency too, but only when it operates in the air. When it is immersed in water or in contact with biological tissues, the membrane movements are extremely damped by the medium that is in contact with the transducer, so it'll no longer oscillate at its distinct resonant frequency, but it can oscillate at the frequency used to drive it [6]. This result allows the capacitive transducer to work over a much broader bandwidth than piezoelectrics: it can emit short ultrasonic pulses at high frequencies for improved image resolution, but it can also be induced to buzz at lower frequencies to go deeper in the body. As a result, by placing 9000 micromachined sensors in a 2D array, Butterfly iQ+ can emulate ultrasound waves produced by any type of transducer (linear, curved or phased), combining three

transducer bandwidths and applications in one single probe, as shown in figures 1.3, 1.4 and 1.5. By eliminating the need of specialized probes, Butterfly iQ+ can be used for whole body imaging, making versatility one of its main valuable characteristics.

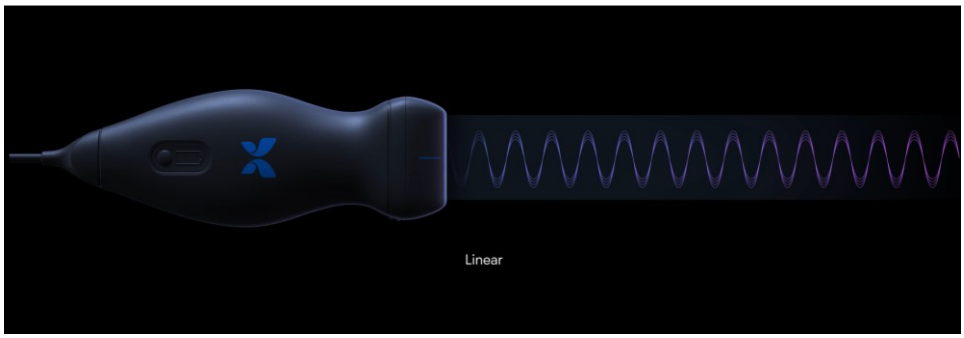

Figure 1.3. Butterfly iQ+ emulating waves produced by linear transducer [7].

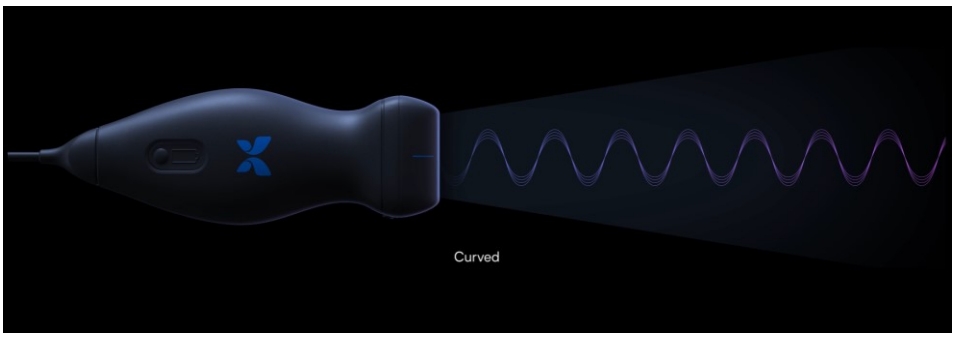

Figure 1.4. Butterfly iQ+ emulating waves produced by convex transducer [7].

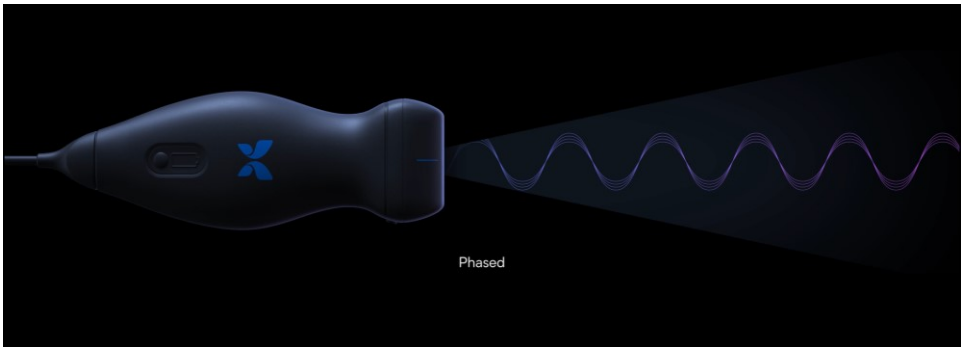

Figure 1.5. Butterfly iQ+ emulating waves produced by phased transducer [7].

1.3 System overview and imaging features

Table 1 lists the technical system specifications for the probe and for the software application [10]:

Butterfly iQ+ system specifications	
Item	**Specification**
Probe dimensions	163 x 56 x 35 mm (6.4 x 2.2 x 1.4 in.)
Probe weight	309 g (0.68 lb)
Power	Battery (rechargeable)
Battery life	≥2 hours in B-Mode (typical new battery at 25°C). ≥2 hours refers to continuous scanning vs. traditional scanning patterns.
Min/Max scan depth	1 cm min / 30 cm max
Ultrasound chip	Integrated CMOS chip
Transducers	~9000-element CMUT
Frequency Range	1-10 MHz
Operating system	• Apple devices require iOS 13.0 or newer. Not compatible with beta or unreleased versions. • Google Pixel devices require Android version 10 or newer. • OnePlus mobile devices require Android version 10 or newer. • Samsung mobile devices require Android version 9 or newer

Table 1.1. System specifications.

Due to its high versatility, Butterfly iQ+ is designed to be used in all areas of medicine. To perform a new scan, once the probe has been connected to the mobile device, it is possible to select from the App interface the correct clinical preset according to the associated body part being examined. Users can select among 21 presets available:

- Abdomen
- Abdomen deep
- Aorta & Gallbladder
- Bladder
- Cardiac
- Cardiac deep
- FAST
- Lung
- MSK – Soft Tissue
- Musculoskeletal
- Nerve
- OB1/GYN
- OB2/3

- Ophthalmic
- Pediatric Abdomen
- Pediatric Cardiac
- Pediatric Lung
- Small organ
- Vascular: access
- Vascular: carotid
- Vascular: deep vein

A series of predefined imaging parameter values is associated to each preset. Once a preset is chosen, Butterfly iQ+ App operates by using the imaging parameters automatically selected, which include, among others, the type of ultrasonic beam, gray-scale, operating frequency and maximum scan depth, all optimized for the anatomy being scanned.

When performing a study, through the App interface it is also possible to adjust the following controls: global gain, scan depth and Time Gain Compensation (TGC) at three depth levels (near, mid, far). Imaging functions include B-Mode, M-Mode, Color Doppler, and Power Doppler. Additional settings comprise functions for measurements and annotations.

Once the acquisitions are completed, ultrasound exams can be uploaded and stored from the Butterfly App into the dedicated Cloud, a data archive always accessible everywhere and from any device. The access to Butterfly Cloud allows users to review all acquired images, to organize them into archives (folders), to add detailed patient information and to share studies with anyone, even in deidentified form, for consultations or remote diagnosis. This potentiates the collaboration among clinicians and the connectivity with traditional medical record systems.

A major potential for Butterfly iQ+ is the incorporation of Artificial Intelligence (AI) technology that provides guidance during both image acquisition and interpretation [11]. AI tools currently available are: automatic Ejection Fraction calculation when using cardiac preset, automatic bladder volume estimation available in bladder preset, and view guidance tools -for educational use only- whose purpose is to provide, through a visual indication, a real-time feedback of the image quality while scanning. View guidance tools support the following views: cardiac apical 4 chambers, parasternal long axis and parasternal short axis in cardiac preset, and A-lines and B-lines in lung preset.

1.4 Pros and cons

There are multiple advantages in the use of Butterfly iQ+, but also certain limitations.

1.4.1 Pros

- Portability: by its nature, iQ+ is a handheld device, so it easily fits into any white coat pocket, and it's ready to be performed at any moment and from multiple different locations (out of the hospitals, emergency departments, wards, outpatients, etc.), giving the possibility to make fast decisions whether in non-urgent situations or in emergencies.
- Cost: the device currently costs $2,399 plus $420/year for the membership fee, that covers annual access to educational videos, unlimited storage, and advanced imaging features; nevertheless, Butterfly iQ+ still works without renewing the subscription, but it won't be possible to upload new images for storage. The low price contrasts the tens (sometimes hundreds) of thousands of dollars required to purchase and maintain sophisticated ultrasound systems together with their multiple transducers.
- Versatility: it is a 3-in-1 device, and with a single transducer that works for three, Butterfly iQ+ can perform whole body imaging by choosing among 20 presets that can be selected according to the proper body organ to examine.
- Ergonomics: although Butterfly iQ+ system is heavier than the transducer of a standard ultrasound machine, due to the fact that all the electronics and technology is located inside it, it is a quite small device with an ergonomic design; it is comfortable and it does not easily slip out of the hands while scanning.
- Battery life: Butterfly iQ+ has its own battery with wireless charging, therefore it doesn't drain the phone battery. Battery life of 2 hours of continuous scanning is reasonable. There are a button and a light pattern on the probe, for checking the battery level.
- Butterfly App: the App is designed to be intuitive and the user interface is easy to navigate; through touchscreen users can easily switch between presets, and quickly select the various settings and commands. Any physician with little guidance at the beginning can start to scan on its own.
- Cloud: image storage system, which gives the possibility of image sharing and network collaboration.
- Artificial Intelligence: as already mentioned, AI tools assist in both image capturing and analysis.
- Constant software updates: they provide regularly updated features and tools.
- Educational videos: users can access to a library of ultrasound tutorial videos taken by trained practitioners, especially designed for novice operators. The clips illustrate how to use the iQ+ for various organ scans, with a proper image acquisition and interpretation.
- Replaceable cable: Butterfly iQ+ new release allows to replace connection cable in case of damages, or when a mobile device with a different connector type needs to be used.

1.4.2 Cons

- Non-removable battery: this is a limitation since it is unclear how a battery replacement operation would cost in case of battery fails rather than the hole unit replacement.
- Internet access required: Butterfly App must connect to the internet every 30 days for ensuring the latest updates; moreover, an internet connection is required to archive studies into Butterfly Cloud.
- Overheating: the long battery life advantage is shadowed by the overheating problem, that may occur with continuous scans.
- Not available features: depending on the geographic location, the membership status, the hardware or the platform, some functionalities are not supported in all Butterfly probes. E.g., some features and settings not tested in this thesis because unavailable are: Teleguidance, a technology used to remotely guide in the use of Butterfly iQ+ through video calls, is only supported on Apple devices, while the probe tested is compatible with Android platform. One of the AI-assisted tools, the automatic Ejection Fraction calculation, is not available on Android devices too. Another major limitation is the absence of Spectral Doppler velocimetry, a graphical functionality that displays blood flow velocity measurements over time. This last ultrasound modality is only available for customers in the United States. It is desirable that in future all these features will be implemented in all probes and in all countries.

There is one fundamental parameter unmentioned neither in the pros nor in the cons, which is the image quality. Even without a good eye it is possible to notice that image quality from images captured by Butterfly iQ+ device is good, but not excellent. Nevertheless, before labeling this important aspect as a disadvantage, a study on a quantitative assessment of image quality has been conducted and better illustrated in Chapter 3.

Chapter 2

State of art

2.1 Evolution of handheld ultrasound devices

In recent years, rapid development of microelectronic industry has been applied to the diagnostic ultrasound field, resulting in the progressive spread of handheld ultrasound systems, supported by the noticeable interest that medical community has reserved for these devices. The advantages provided by such pocket-sized devices, that are the possibility to bring ultrasounds to any patients anywhere and at any time, have attracted great attention from doctors and clinicians.

2.1.1 Early handheld ultrasound systems

First products have been developed in the United States starting from the late 1990s. They were not handheld yet, but only portable. SonoSite developed the first portable ultrasound equipment, with the advantage of being small, stable, and with reduced volume and weight, compared with standard ultrasound machines. In the early 2000s, a new generation of portable color ultrasound machines was launched by the company with improved processing performances, like MicroMaxx, M-Turbo and S-Series. Meanwhile, representative products in China appeared for the first time in 2002, thanks to WellD company that produced a range of handheld black and white ultrasound devices whose volume was comparable to the size of a book. Products like WED-2000, WED-2000A, WED-3000, WED-3100 and WED-2018 could be configured with ten different type of probes.

2.1.2 Current handheld ultrasound systems

Nowadays, several handheld ultrasound devices approved for clinical applications currently represent the major competitors to Butterfly iQ+ system in the portable ultrasound market. One of these products is Vscan (General Electric, USA), a handled ultrasound device launched in 2008. Its battery guarantees 1 hour of continuous use and its new version provides a dual probe, that means that houses two transducers (linear and curvilinear) in the same probe, in order to extend the range of clinical applications (figure 2.1).

Figure 2.1. GE Vscan device [12].

Another ultrasound handheld device is Lumify system (Philips, USA), launched in 2015. Unlike the previous scanner, its transducers connect to a smartphone or tablet to display images. It can be equipped with three types of probes: linear, curvilinear and phased (figure 2.2).

Figure 2.2. Philips Lumify system [13].

Clarius scanner (Clarius Mobile Health, CA) developed in Canada has the advantage of being wireless. Like Lumify, it is smartphone based. There are various scanners with different transducers specialized for different frequency ranges and clinical applications (figure 2.3).

Figure 2.3. Clarius wireless scanner [14].

Chinese company SonoStar (SonoStar Technologies, Guangzhou, China) has produced its own wireless ultrasound system too (figure 2.4).

Figure 2.4. SonoStar wireless device [15].

A summary of competitors to Butterfly iQ+ device in the portable handheld ultrasound market is listed in table 2.1 [16].

Handheld ultrasound devices				
Name	**Probes**	**Link**	**Technology**	**Company**
Vscan Exend	Dual probe (linear and curvilinear)	Cable	Piezoelectric crystals	GE Healthcare, USA
Lumify	Linear, curvilinear, phased array	Cable	Piezoelectric crystals	Philips, USA
Clarius	Several specialized probes, among linear, convex, microconvex, phased, endocavity	Wireless	Piezoelectric crystals	Clarius, CA

SonoStar	Linear, Convex, microconvex, phased, endocavity and double heads series	Wireless	Piezoelectric crystals	SonoStar, China
Butterfly iQ+	3-in-1 (linear, curvilinear, phased in single probe)	Cable	CMUT-based	Butterfly Network, USA

Table 2.1. Main handheld ultrasound devices currently available.

Some of these devices include notable features not available in Butterfly iQ+, like the possibility to perform Spectral Doppler or the wireless transmission between the ultrasound system and its coupled mobile device, that allows easier movements around the workspace and avoids the risks of cord damages and infections. Nevertheless, from a cost perspective no other handheld ultrasound device on the market has 3-in-1 transducer like Butterfly iQ+ has, leading to considerably increase their costs.

Chapter 3

Image quality assessment in Butterfly iQ+ system

3.1 Introduction

Progressive degradation of ultrasound systems due to their use can interfere on image quality, producing errors in diagnostic decision making. For this reason, the importance of monitoring image quality in ultrasound is widely recognized, and quality control programs are recommended by the most important scientific associations. The aim of this chapter is to analyze the performances of Butterfly iQ+ system through a quantitative assessment of a series of parameters related to image quality in ultrasound. A traditional ultrasound machine has been tested too, maintaining the same settings for a comparison. The experimental work can be divided into two steps: a first part of acquisition of all ultrasound images, by scanning a commercial phantom through which all necessary tests for image quality assessment have been performed, and a second part of image analysis, where the measurement, calculation or visual evaluation of image quality indicators have been conducted. The analysis has been performed mainly with MATLAB software (MathWorks Inc., Natick, MA, USA). Results of the tests have been used firstly for the evaluation of accuracy, to monitor any potential value that could exceed the suggested tolerance limits, and secondly for a statistical analysis by means of a paired-sample t-test, to see if, for each test, performances of Butterfly iQ+ could be considered congruent to that of standard ultrasound system or not.

3.2 Equipment used

Ultrasound phantom is a precision tool used to perform the fundamental tests that assess image quality of an ultrasonic system over time. In this study it has been used the General-Purpose Ultrasound Phantom, Model 054GS (shown in figure 3.1), manufactured by CIRS (Computerized Imaging Reference Systems Inc.). This phantom is filled with a material called Zerdine®, a solid elastic hydrogel that simulates the acoustic properties of human soft tissue. The external housing is made of rugged ABS plastic, for added durability, while the scanning surface -placed on the top- is a skin-like membrane made of composite laminate. Coupling gel can be applied directly to the scan surface, to prevent air pockets and ensure a good transmission of ultrasound beam.

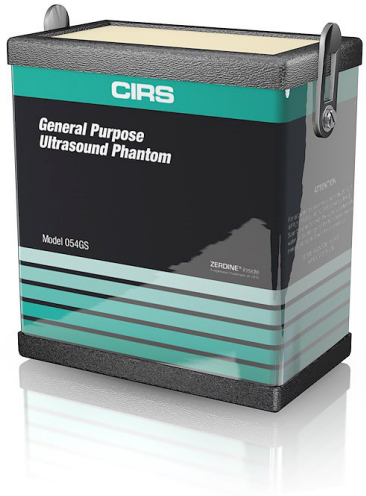

Figure 3.1. CIRS General-Purpose Ultrasound Phantom. Model 054GS [17].

For testing several image quality indicators, the phantom contains various objects such as reflecting targets made of nylon monofilament, anechoic cylinders and gray scale targets, immersed inside the tissue-mimicking material. General characteristics of CIRS Model 054GS phantom are summarized here in table 3.1 [17]:

CIRS Model 054GS phantom	
Physical specifications	
Phantom weight	11 lb (4.1 kg)
Phantom housing	
Material	ABS Plastic
Outer Dimensions	17.8 cm x 12.7 cm x 20.3 cm (7” x 5” x 8”)
Scanning surface	
Material	Saran-based laminate
Dimensions	14 cm x 9 cm (5.5” x 3.5”)
Background material	
Material	Zerdine®

Speed of sound	1540 m/s
Freezing point	0° C
Melting point	Above 100° C
Attenuation coefficient	0.5 dB/(cm·MHz)
Other	Compatible with harmonic imaging
Wire targets	
Material	Nylon monofilament

Table 3.1. CIRS 054GS phantom general characteristics.

Targets are grouped and located at various depths inside the phantom, and they can be observed by moving the transducer across the scanning surface. A complete view of all detectable targets is shown in figure 3.2 and further details are specified in table 3.2 below. All measurements are made at 22°C ± 1°C.

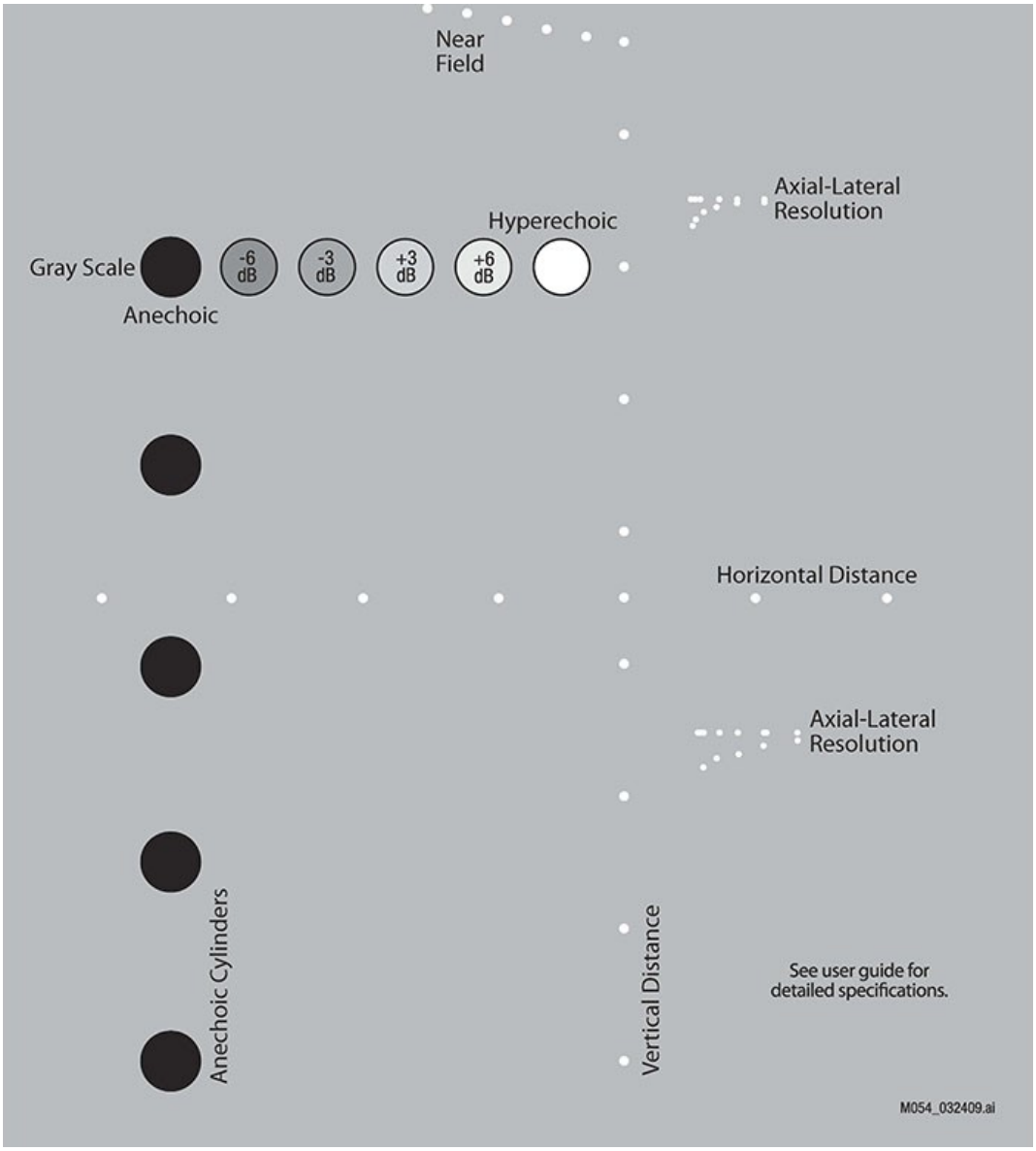

Figure 3.2. Schematic of targets embedded in CIRS phantom - Model 054GS [18].

CIRS phantom targets	
Near field group	
Number of targets	6
Diameter	100 µm
Depth range	1 to 6 mm
Vertical distance between targets	1 mm
Vertical distance group	
Number of targets	8
Diameter	100 µm
Depth range	2 to 16 cm
Vertical distance between targets	20 mm
Horizontal distance group	
Number of targets	7
Diameter	100 µm
Depths	9 cm
Horizontal distance between targets	20 mm
Axial-Lateral resolution groups	
Group 1:	
Diameter	80 µm
Depths	3 cm
Axial & Lateral separation between targets	4, 3, 2, 1, 0.5 & 0.25 mm
Group 2:	
Diameter	80 µm
Depths	11 cm
Axial & Lateral separation between targets	5, 4, 3, 2 & 1 mm
Anechoic cylinders	
Material	Zerdine®
Number of cylinders	5
Contrast	Anechoic
Diameter	8 mm
Depths	4, 7, 10, 13 & 16 cm
Gray scale targets	
Material	Zerdine®
Number of targets	6
Contrasts	Anechoic, -6 dB, -3 dB, +3 dB, +6 dB & hyperechoic, with respect to background
Diameter	8 mm
Depth	4 cm

Table 3.2. CIRS phantom targets.

3.3 Phantom study

In this paragraph are described the procedures useful to evaluate a series of parameters related to a quantitative and objective image quality assessment of ultrasound images. This study has been conducted in collaboration with Dr. F. Ribero. Parameters have been evaluated by means of tests carried out with the CIRS 054GS phantom, provided by Politecnico of Turin. Each test is related to a different group of targets that can be detected by a phantom scanning.

In this context, Butterfly iQ+ has been tested with a phantom study, but also compared performing the exact same experiments with another ultrasound system. The other equipment tested is a standard ultrasound machine, Philips Affiniti 30 (Philips Ultrasound, Bothell, WA, USA; L 12-4 and C 6-2 probes). The aim of these tests is to compare the B-mode image quality of Butterfly iQ+ with a conventional ultrasound equipment.

For each ultrasound system, the following parameters have been evaluated:

- Vertical distance measurement
- Horizontal distance measurement
- Anechoic objects imaging
- Dead zone
- Axial resolution
- Lateral resolution
- Image uniformity
- Contrast response

It is important to outline that these procedures made on both equipment are simple tests with the goal of verifying a good functionality, so they are not considered as periodic examinations being part of a Quality Control program, since Butterfly iQ+ system is unused and not degraded yet. They are just one-off tests carried out to compare Butterfly iQ+ performances with results obtained from a traditional ultrasound machine.

Nevertheless, before comparing two systems, their performances in turn must be compared to some reference value, to quantify measurement accuracy and evaluate if any deviation from reference value is allowable or not. Usually, in routine Quality Control tests, the reference values are the first set of measurements taken, and they are recorded as baseline measurements, in order that all subsequent tests will be compared with baseline results. Any deviation from original values is evaluated and quantified, and if the difference exceeds a specific threshold, it means that a significant change in image quality has occurred and a corrective action for the ultrasound system is required. In this work of thesis instead, the values used as references will be those stated

in the phantom specifications listed in table 3.2. Even if these image quality tests don't follow any Quality Control program, tolerance values used in this study to quantify measurements accuracy are taken from standards published by American Association of Physics in Medicine (AAPM) report [19].

The report specifies two different thresholds for evaluating allowable deviations from reference value (figure 3.3). If measurement values exceed maximum acceptable error, tolerance limits are crossed and defective quality levels are reached. For this reason, it is better to take a corrective action if image quality indicators exceed a more restrictive threshold, before reaching defect levels. This inner threshold is called action level, it is usually set at 75% of tolerance limits, and it ensures that any measurements value included in the normal operating range delimited by action levels, can be considered acceptable and sufficiently near to reference value, which is the expected value to obtain.

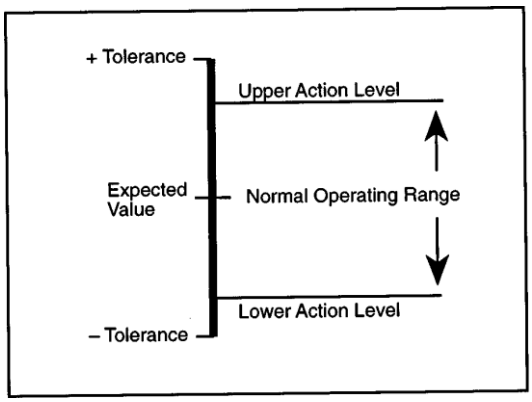

Figure 3.3. Action and defect levels [19].

For example, if the vertical distance between two reflecting pins is 20 mm according to phantom specifications for vertical distance measurement, 20 mm will be the reference value. If the maximum acceptable error is ±2%, it equals to 20·0.02=0.4 mm, while the action level is set at 75% of tolerance limits, so its range is 0.4·0.75=0.3 mm. Therefore, the ultrasound system may detect 20 mm as being anywhere from 19.7 mm to 20.3 mm and still be functioning properly.

Table 3.3 provides suggested action and defect levels for the image quality indicators tested in this study, even if, according to AAPM report, they are not inflexible standards.

Image quality indicator	**Suggested defect level**	**Suggested action level**
Image uniformity	Nonuniformity ≥6 dB	Nonuniformity ≥4 dB
Vertical distance accuracy	Error ≥2 mm or 2%	Error ≥1.5 mm or 1.5%
Horizontal distance accuracy	Error ≥3 mm or 3%	Error ≥2 mm or 2%

Axial resolution	In general >1 mm, or any consistent measurable change from baseline	> 1 mm for central frequencies greater than 4 MHz, or > 2 mm for central frequencies less than 4 MHz
Lateral resolution	Change <1.5 mm from baseline value	> 1.5 mm for transducer frequency (f) ≥ 5 MHz, or > 4 mm for f < 5 MHz
Dead zone	10 mm for f < 3 MHz 7 mm for 3 MHz < f < 7 MHz 4 mm for f ≥ 7 MHz	7 mm for f < 3 MHz 5 mm for 3 MHz < f < 7 MHz 3 mm for f ≥ 7 MHz
Anechoic object imaging	Major distortion or any consistent measurable change from baseline	Major distortion or any consistent measurable change from baseline

Table 3.3. Criteria for evaluation of test results.

From this list of parameters contrast is not included, since the AAPM report does not provide any criterium for accuracy evaluation of this test's results. In absence of recommended tolerance limits for contrast response, it has been decided to consider results obtained from this work of thesis as new baseline values to compare with future possible tests.

3.3.1 Conditions for the assessment of image quality

Results of the measurements and, more generally, the evaluation of parameters related to image quality assessment strongly depend on system settings used during the phantom scanning. For both equipment, it is important to establish and record the same system settings for each of the image quality tests. In particular, the same following conditions should be employed while performing tests with both Butterfly iQ+ and standard ultrasound system:

- preset (body part selection);
- scan depth;
- gain level;
- time gain compensation (TGC).

If different settings are used, the results may not be valid. Further settings available for traditional device but not for Butterfly iQ+, including dynamic range and focal zone depth, may be adjusted by clinician assisting with acquisitions, if necessary.

For each image quality parameter tested, another condition is that each ultrasound system must acquire multiple images of the same target, by varying, as much as possible and whenever it's

necessary, 3 different presets (vascular-carotid, small organ, aorta & gallbladder), 3 different image depths and 3 different gain levels, one setting at a time.

3.3.2 Description of image quality parameters and acquisition protocol

Vertical distance measurement

Vertical distance test is useful to perform a depth calibration and assess the accuracy of measurements along the axis of the beam. The depth of an acoustic interface with respect to the transducer surface can be determined by measuring the time of flight of the ultrasonic pulse (elapsed time between pulse transmission and echo registration). With the assumption that the speed of ultrasound in tissues is constant (1540 m/s), it is possible to calculate the location of the echo by converting measured time into a distance. Vertical distance errors can be caused by a failure in the system's internal timing circuits, or by the fact that velocity of ultrasound in the phantom material may not be equal to that in tissues, since it is sensitive to temperature fluctuations.

Phantom section for this test includes a column of eight nylon monofilament wires, vertically spaced at 20 mm intervals. When performing the scan with the transducer, pressure on the phantom surface must be avoided to prevent any distortions in the image, that could cause incorrect distances to be measured. With a computer analysis, distances between each couple of contiguous wires at various depths have been measured. Distance accuracy is then evaluated by comparing distance measurements with known distances provided by the phantom specifications.

Vertical distance testing procedures

- Apply coupling gel to the scanning surface.
- Position the transducer of the standard ultrasound system above the vertical column of filament targets (wires should appear as dots, not lines).
- Scan the region in the phantom so that vertical distance group of targets appears toward the center of the image.
- Adjust the following instrument settings, by varying them one setting at a time:
  - Preset: aorta & gallbladder;
  - Depth: 18 cm;
  - Gain: 80%, 85%, 90%.
- Freeze one image for each different setting combination and obtain a hard copy.
- Computer analysis: measure the distances between two adjacent wires at various depths and record these measurements.
- Repeat above procedures for Butterfly iQ+ system.

- Compare results of two devices.

Horizontal distance measurement

Horizontal distance test determines the accuracy of measured distances along lateral direction, perpendicular to the beam axis. Errors in horizontal distance measurements can be the results of flaws in the scan mechanism, especially in mechanical transducers, in which the motor wear can have an impact on the acquisition timing of each line of sight of the B-mode image [20].

Targets in the phantom reserved for this quality test consist of a set of seven horizontal nylon wires with a 20 mm gap between them. With a computer analysis, distances between each couple of contiguous wires have been measured. In the same way as made in vertical distance procedure, the accuracy of measurements is assessed by comparing distance measurements with the actual distance between the line targets in the phantom.

Horizontal distance testing procedures

- Apply coupling gel to the scanning surface.
- Position the transducer of the standard ultrasound system in a vertical plane (wires should appear as dots, not lines).
- Scan the region in the phantom so that horizontal targets are all visible.
- Adjust the following instrument settings, by varying them one setting at a time:
  - Preset: aorta & gallbladder;
  - Depth: 12 cm, 14 cm;
  - Gain: 70%, 75%, 80%.
- Freeze one image for each different setting combination and obtain a hard copy.
- Computer analysis: measure the distances between two adjacent wires along the horizontal plane and record these measurements.
- Repeat above procedures for Butterfly iQ+ system.
- Compare results of two devices.

Anechoic objects imaging

The ability to detect and accurately represent round, negative contrast, anechoic structures is a very important feature for an ultrasound system. It is especially critical in many clinical applications such as breast and liver imaging, as it determines the ability to detect cysts or lesions. Nevertheless, in ultrasonography the word “cystic” used for naming anechoic cyst-like structures does not only refer to cysts, but it is also used to describe any fluid-filled object [21], such as

urine, bile, water, blood vessels, which are all examples of anechoic structures. Anechoic objects imaging can be affected by the presence of electronic noise, side lobes of the beam, and problems in the image processing hardware.

The ability of an ultrasound machine to properly represent masses can be determined using the phantom section including five anechoic cylinders located at various depths. Their shape (they should appear round), the edges (sharpness), and the interior (anechoic) are three parameters used to qualitatively grade the accuracy of representation of anechoic objects. There is no standardization for these structures that are subjects to be measured, so tolerance limits on a quantitative scale cannot be defined yet [22]. For this reason, criteria based on APPM report for this test simply suggest comparing results with baseline values (results obtained during the first test). In this work of thesis, only the shape of anechoic structures has been tested, in particular the evaluation of geometric distortion by measuring the Aspect Ratio. Aspect Ratio is the ratio between height of the object divided by its width. Since cross sections of cylindrical anechoic structures are circular, the height and width should be the same and it's desirable that Aspect Ratio tends to 1. Without tolerance limits provided by APPM report for this test, a suggested acceptance criterion [19] considers taking a corrective action if the anechoic objects display major distortion, that is more than 20% of difference between their height and width.

Anechoic objects testing procedures

- Apply coupling gel to the scanning surface.
- Position the transducer of the standard ultrasound system above the vertical column of anechoic cylinders and in a perpendicular plane, to image their circular cross section.
- Scan the region in the phantom containing the anechoic cylinders.
- Adjust the following instrument settings, by varying them one setting at a time:
  - Preset: aorta & gallbladder;
  - Depth: 18 cm;
  - Gain: 80%, 85%, 90%.
- Freeze one image for each different setting combination and obtain a hard copy.
- Computer analysis: measure the height and the width of each anechoic cylinder and record their ratio as Aspect Ratio.
- Repeat above procedures for Butterfly iQ+ system.
- Compare results of two devices.

Dead zone

Dead zone (also called Ring-down distance) is the distance from the front face of the transducer to the first identifiable echo. It's a region in the ultrasound image where no useful information

can be collected because it's too close to the transducer surface. This zone occurs because the ultrasound system cannot transmit and receive data simultaneously, and since each emitted pulse has finite length, echoes from low depth may not be detected if they coincide in time with the excitation pulse [20], that is when the transducer it's not ready to receive signals. As pulse frequency increases, pulse length decreases, and dead zone becomes shorter. A change in dead zone amplitude is indicative of a problem with the ultrasound transducer, the electronic pulse system or both.

Dead zone control test is done with the near field group, the group of targets closest to the phantom scanning surface. It is composed of six parallel monofilament wires, horizontally spaced 6 mm apart from center to center (figure 3.4). First target is positioned 1 mm below the scan surface, subsequent targets are spaced with 1 mm increments, up to 6 mm of depth.

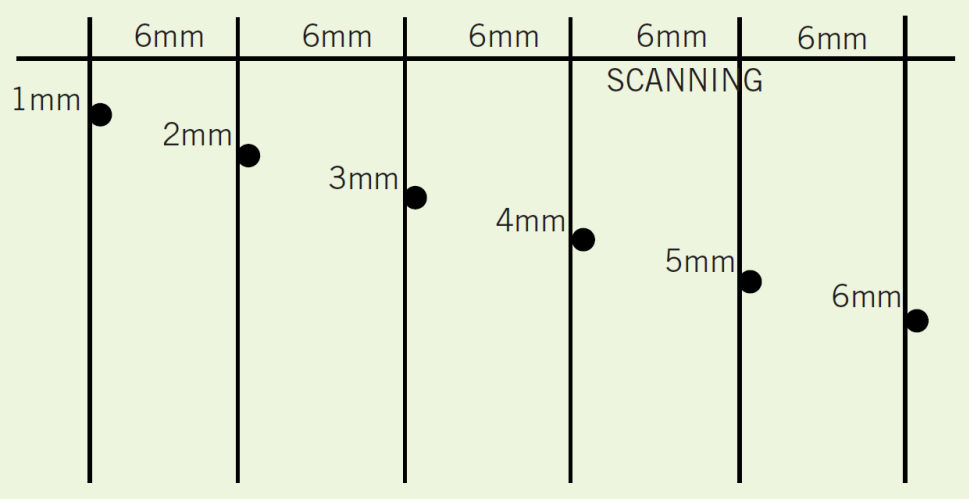

Figure 3.4. Near field group [18].

An estimate of the dead zone can be obtained by examining the most superficial target that can be unequivocally identifiable. For example, if the first target observed is located at 2 mm away from the phantom top surface, then the dead zone distance is considered "something less than 2 mm". In this case it has also been measured the distance between the scan surface and the first target imaged, to get a measured value of the dead zone.

Dead zone testing procedures

- Apply coupling gel to the scanning surface.
- Position the transducer of the standard ultrasound system above the near field group and perpendicular to the wires that should appear as dots, not lines.
- Scan the region in the phantom containing the near field group.
- Adjust the following instrument settings, by varying them one setting at a time:
  - Preset: vascular-carotid, small organ;
  - Depth: 3 cm;

    - Gain: 50%, 60%, 70%.
- Freeze one image for each different setting combination and obtain a hard copy.
- Identify the closest wire of the near field target that can be seen.
- Computer analysis: measure the depth of the closest visible target and record this as dead zone.
- Repeat above procedures for Butterfly iQ+ system.
- Compare results of two devices.

Axial and lateral resolution

Spatial resolution is defined as the ability to detect the nearest couple of adjacent objects which could be clearly identified as separate in the image, and by recording the distance between the objects [20]. In other words, how close can two objects be and still be detected as two distinct objects? Objects can be defined as separate when a dark line exists between them. If a system has a poor resolution, small structures lying close to each other will appear as one entity.

In particular, axial resolution regards objects located along the axis of the ultrasound beam, while lateral resolution is concerned with the direction perpendicular to the beam axis. The resolution in the axial direction is limited by the length of the ultrasound pulse, which in turn depends on the center frequency. The higher the frequency, the shorter the pulse length and the better the axial resolution. Lateral resolution is approximately equal to beam width, and depends on depth, focal zone, gain and sensitivity settings. It can be affected by malfunction of transducer elements or by problems in the beam forming system.

Axial and lateral resolution tests are evaluated on two target groups, placed at two different depths. First group is located at 3 cm depth, for the evaluation of probes of 5 MHz and above. It is composed of thirteen line targets, labeled from A1 to A7 and from B1 to B6 to assess respectively axial and lateral resolution, as shown in figure 3.5.

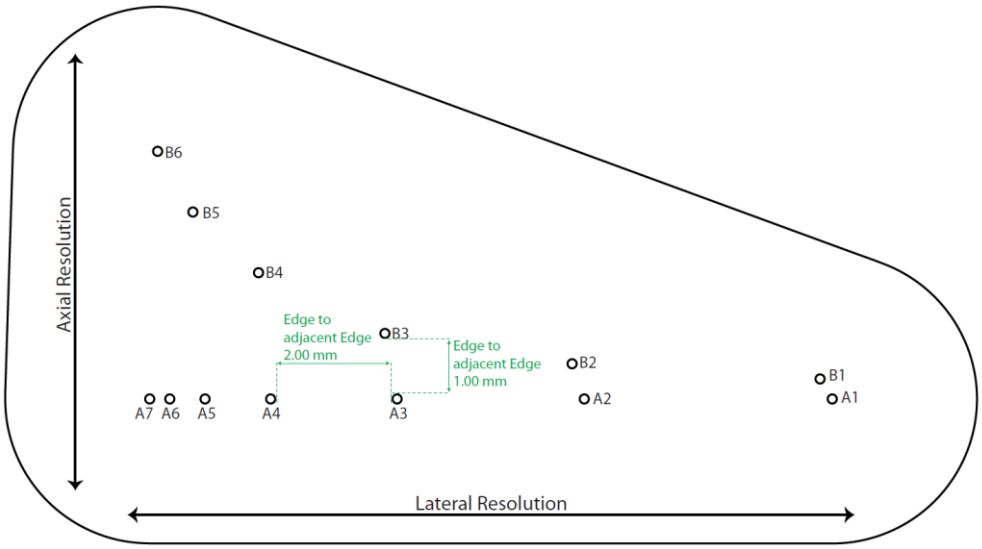

Figure 3.5. Combined Axial/Lateral resolution targets at 3 cm depth [18].

Lateral resolution wire targets are horizontally spaced at 0.25, 0.5, 1.0, 2.0, 3.0 and 4.0 mm intervals from edge to edge. Each of them (except for target A7) is also vertically coupled with an axial resolution reflector, creating pair of targets separated by distances of 4.0, 3.0, 2.0, 1.0, 0.5 and 0.25 mm. Table 3.4 presents various distances associated to each pair of wires, both in axial and lateral direction, useful to assess distance resolution.

	Targets					
	A1-B1	**A2-B2**	**A3-B3**	**A4-B4**	**A5-B5**	**A6-B6**
Axial resolution (mm)	0.25	0.5	1.0	2.0	3.0	4.0
	A1-A2	**A2-A3**	**A3-A4**	**A4-A5**	**A5-A6**	**A6-A7**
Lateral resolution (mm)	4.0	3.0	2.0	1.0	0.5	0.25

Table 3.4. Assessing distance resolution for targets at 3 cm depth.

Second group of targets is placed at 11 cm depth and is designed for low frequency probes. It consists of eleven nylon wires, labeled from C1 to C6 to assess the lateral resolution and from D1 to D5 to assess the axial resolution, as presented in figure 3.6.

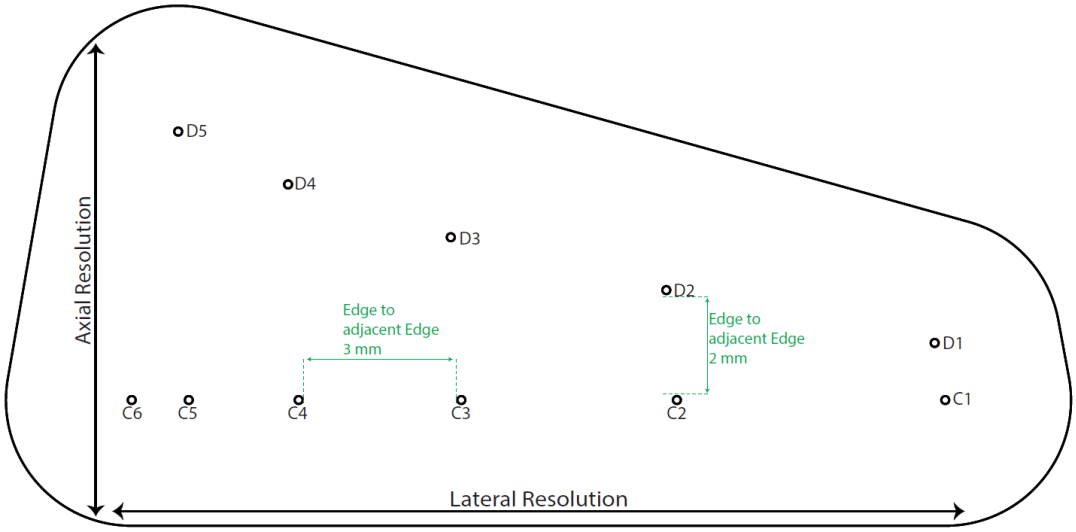

Figure 3.6. Combined Axial/Lateral resolution targets at 11 cm depth [18].

Each pair of line targets is spaced at 1.0, 2.0, 3.0, 4.0, and 5.0 mm intervals, both in axial and in lateral direction. Table 3.5 shows distances separating each pair of wires for this second group of targets.

	Targets				
	C1-D1	**C2-D2**	**C3-D3**	**C4-D4**	**C5-D5**
Axial Resolution (mm)	1.0	2.0	3.0	4.0	5.0
	C1-C2	**C2-C3**	**C3-C4**	**C4-C5**	**C5-C6**
Lateral Resolution (mm)	5.0	4.0	3.0	2.0	1.0

Table 3.5. Assessing distance resolution for targets at 11 cm depth.

Resolution in axial and lateral directions is estimated without making any measurements or calculation, differently from the other image quality control tests made in this study. It is just evaluated by visually examining the acquired image, and defining the minimum distance between the last two closely spaced targets that can be imaged separately.

Axial resolution testing procedures

- Apply coupling gel to the scanning surface.
- Position the transducer of the standard ultrasound system in a vertical plane (wires should appear as dots, not lines).
- Scan the region in the phantom containing the axial and lateral resolution targets placed at 3 cm depth.
- Adjust the following instrument settings, by varying them one setting at a time:
  - Preset: aorta & gallbladder, vascular-carotid, small organ;

    - Depth: 5 cm and 14 cm (for aorta & gallbladder preset), 4 cm (for vascular-carotid and small organ presets);
    - Gain: 70%, 75% and 80% (for aorta & gallbladder preset), 45%, 50%, 55% (for vascular-carotid and small organ presets).
- Freeze one image for each different setting combination and obtain a hard copy.
- Identify the last pair of wires to be distinguished as two distinct structures, along the axis of the ultrasound beam, and refer to table 3.4. Record the distance separating above mentioned pair of wires as axial resolution.
- Repeat for filament targets of interest at 11 cm depth.
- Repeat above procedures for Butterfly iQ+ system.
- Compare results of two devices.

Lateral resolution testing procedures

- Apply coupling gel to the scanning surface.
- Position the transducer of the standard ultrasound system in a vertical plane (wires should appear as dots, not lines).
- Scan the region in the phantom containing the axial and lateral resolution targets placed at 3 cm depth.
- Adjust the following instrument settings, by varying them one setting at a time:
    - Preset: aorta & gallbladder, vascular-carotid, small organ;
    - Depth: 5 cm and 14 cm (for aorta & gallbladder preset), 4 cm (for vascular-carotid and small organ presets);
    - Gain: 70%, 75% and 80% (for aorta & gallbladder preset), 45%, 50%, 55% (for vascular-carotid and small organ presets).
- Freeze one image for each different setting combination and obtain a hard copy.
- Identify the last pair of wires to be distinguished as two distinct structures, along the lateral direction, and refer to table 3.4. Record the distance separating above mentioned pair of wires as lateral resolution.
- Repeat for filament targets of interest at 11 cm depth.
- Repeat above procedures for Butterfly iQ+ system.
- Compare results of two devices.

Image uniformity

Ultrasound image uniformity is defined as the equipment ability to display the speckle of a same tissue in a homogeneous way within the field of view or some of its parts [23]. Consequently, areas where speckle patterns are significantly different from their neighbors, are non-uniform

regions. Uniformity is a good test to ensure that all lines of sight from all crystals within the transducer are properly functioning. Alternatively, other causes of nonuniformities may be poor electrical contacts in cables, software bugs or failures in the image processing circuitry. The presence of nonuniformities may mask subtle variations in tissue texture, increasing the risk of false negatives, and at the same time they may lead to the diagnosis of non-existent pathologies. Although uniformity is an important image quality indicator to evaluate the performances of an ultrasound system, this parameter is often assessed from a qualitative point of view, through a visual inspection of the image and by using subjective criteria. Nevertheless, it is also possible to give an objective assessment of the image uniformity, according to a definition based on separation into Regions of Interest (ROI) on the image [22], [24], [25].

Uniformity testing procedures

- Apply coupling gel to the scanning surface.
- Position the transducer of the standard ultrasound system above a phantom region free of targets and containing only speckle pattern.
- Adjust the following instrument settings, by varying them one setting at a time:
  - Preset: aorta & gallbladder, vascular-carotid, small organ;
  - Depth: 5 cm, 10 cm, and 14 cm (for aorta & gallbladder preset), 3 cm and 6 cm (for vascular-carotid and small organ presets);
  - Gain: 75%, 80% and 85% (for aorta & gallbladder preset), 50%, 60%, 70% (for vascular-carotid and small organ presets);
- TGC: to be adjusted in order that the background is as uniform as possible.
- Freeze one image for each different setting combination and obtain a hard copy.
- Computer analysis: position along the axial direction a series of 4 ROI of small dimensions. Compute average pixel value ($\overline{PV}_i$, i=1,…,4) in each ROI. Compute the difference between the average pixel values of the two quadrants with the highest (MAX($\overline{PV}_i$)) and lowest (min($\overline{PV}_i$)) average pixel values, and record this result as uniformity parameter:

  $$U = MAX(\overline{PV}_i) - min(\overline{PV}_i)$$

  which is equal to the maximum variation of mean grey levels among discrete quadrants. To compare results with tolerance limits suggested by international standards, uniformity has been converted in decibel scale.
- Repeat above procedures for Butterfly iQ+ system.
- Compare results of two devices.

Contrast response

The concept of contrast in ultrasound images refers to the ability to distinguish between adjacent structures with different echo intensities. Hence, it is related to the capacity of an ultrasound system to discern tissues having different characteristics. Contrast enhancement can be achieved by increasing differences in brightness between regions in the image.

Targets belonging to gray scale group are used for evaluating contrast. There are six cylinders, in cross-section appearing as discs, with varying degrees of contrast ranging from anechoic to hyperechoic (<-15 dB, -6 dB, -3 dB, +3 dB, +6 dB, >+15 dB) with respect to the background. For this test, absolute criteria are not available. Other international scientific documents similar to AAPM report for quality control procedures in ultrasonography suggested, through a visual assessment of the image, to count the number of cylindrical structures clearly visible, and established as "cut-off value" more than four cylinders identifiable to pass the test. Despite that, even if not specified, it has been chosen to quantitatively evaluate contrast by assessing the gray level difference between each cylinder and background. Differences in the echogenicity of each target have been calculated as the ratio between the mean of the gray levels within the target and the mean of the gray levels of the adjacent background, and then converted to dB scale in order to compare results with nominal contrast values.

Contrast testing procedures

- Apply coupling gel to the scanning surface.
- Position the transducer of the standard ultrasound system in a vertical plane (wires should appear as dots, not lines).
- Scan the region in the phantom so that gray scale targets are visible.
- Adjust the following instrument settings, by varying them one setting at a time:
  - Preset: small organ;
  - Depth: 5 cm;
  - Gain: 60%, 65%, 70%.
- Freeze one image for each different setting combination and obtain a hard copy.
- Computer analysis: fit a circular region of interest (ROI) inside the displayed target, and another circle of the same size as before to select the adjacent background. Compute average pixel value within both ROIs selected, and calculate contrast of each target with respect to background as follows [26]:

$$C_{dB} = 10 \cdot \log_{10}\left(\frac{S_i}{S_o}\right)$$

  where S_i and S_o are the average gray level respectively of the ROI inside the target and the ROI selected for the background. Compute contrast for each echogenic target.
- Repeat above procedures for Butterfly iQ+ system.
- Compare results of two devices.

3.4 Phantom image analysis

3.4.1 Image renaming

Once the acquisition of images through phantom scanning was completed, the study proceeded on MATLAB with the implementation of algorithms useful to analyze images and perform all measurements required. First of all, images have been renamed for an easy and immediate recognition of settings used. Each image name is composed by a letter followed by two numbers, e.g. “C_3_60”, indicating respectively the preset used, the scan depth in centimeters, and the gain level in percentage. Letter referred to preset may be A, C or T:

- “A” stands for aorta & gallbladder preset;
- “C” stands for vascular-carotid preset;
- “T” stands for small organ (thyroid) preset.

3.4.2 Calibration factors assessment

To perform distance measurements for some tests on images acquired during phantom scanning, the knowledge of calibration factor (CF) is required. In fact, calibration factor (mm/pixel) is a fundamental parameter in digital images, because it provides a pixel-to-distance conversion and allows to measure real dimensions rather than just pixels. Basically, it is a number saying ‘how many mm equal one pixel’. Images acquired with traditional ultrasound device are available in DICOM format, therefore the information about calibration factor value is already available. For Butterfly iQ+ instead, a manual calibration has been performed to get a calibration factor estimation.

To calibrate images on MATLAB, objects of known size have been measured, in particular the depth scale in centimeters at the side of each ultrasound image. The creation of two datatips on two bars of the depth scale that are a known distance apart, showed their coordinates, so it was possible to calculate the distance in terms of pixels. Given the length of the measured feature and the distance in pixels, calibration factor can be estimated, and “real” measurements can be easily made.

Manual calibration has been carried out over Butterfly iQ+ images with different scan depths, those requested in the acquisition protocols. All calibration factors estimated are listed in table 3.6.

Calibration factor (mm/pixel)	**Scan depth of the images (cm)**
0.0288	3

0.0385	4
0.0481	5
0.0578	6
0.0961	10
0.1149	12
0.1351	14
0.1724	18

Table 3.6. Calibration factors for Butterfly iQ+ images.

3.4.3 Results of the tests

Results from image quality tests such as vertical and horizontal distance and anechoic object imaging have been compared with real values provided by phantom documentation. During the tests, measurements have been performed more than once for each ultrasound system and for each target examined, since combination of settings has led to the acquisition of more than one image. Therefore, over this group of measured values collected for each group of images, the mean and standard deviation have been computed. Subsequently, absolute error in terms of deviation from reference value has been calculated by taking the difference between mean measured value and known actual value:

$$E = X_m - X_{ref}$$

Absolute measurement error may be positive or negative.

For other parameters, such as dead zone assessment, axial and lateral resolution, and image uniformity, reference values are not provided, so the possible passing of the tolerance limits is the only control made for these tests. Lastly, contrast response test does not have a suggested action level, therefore results of this performance may eventually be saved as baseline values for further tests on Butterfly iQ+ device.

Are now described the procedures of evaluation of each image quality parameter and relative results.

Vertical distance measurement

From phantom specifications listed in table 3.2, it is known that reference value is the vertical distance between two consecutive targets, equal to *20 mm*. Action level suggested for this test corresponds to *1.5 mm*.

Combination of settings according to acquisition protocol has led to the acquisition of three images. Only aorta & gallbladder preset has been used, since it was the only preset with convex beam, that could explore even targets located at high depth in the images. An example of

measurement made on MATLAB between two adjacent vertical targets is shown in figures 3.7 and 3.8. All ultrasound images illustrated have been acquired with Butterfly iQ+ system for this work of thesis.

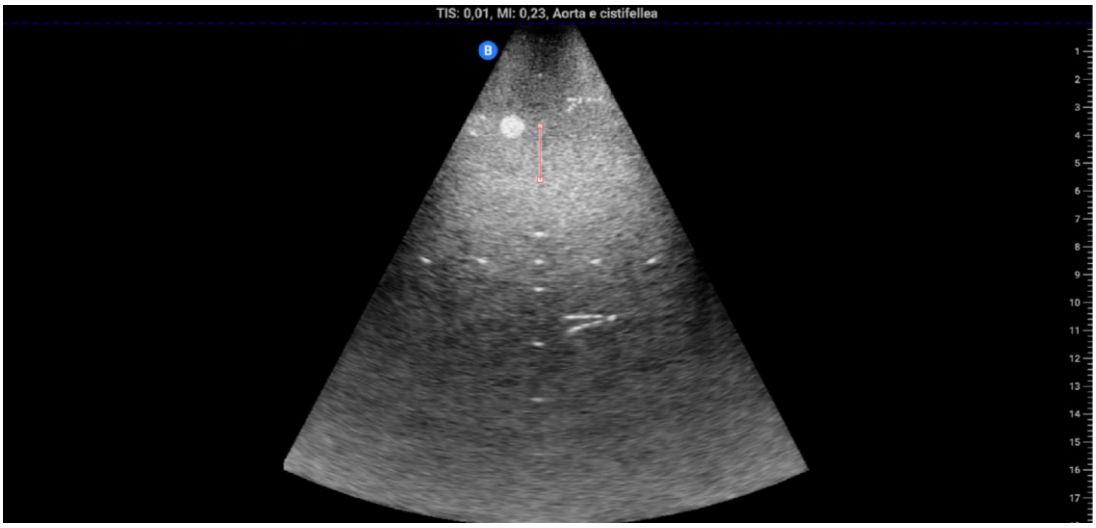

Figure 3.7. Example of vertical distance measurement between two targets on an image.

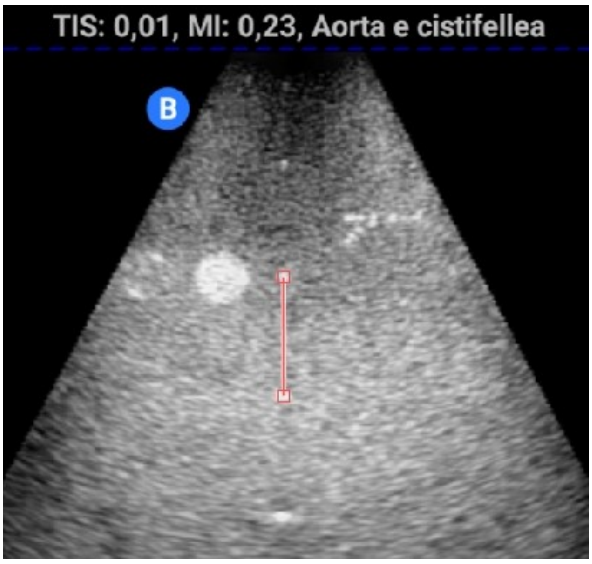

Figure 3.8. Example of vertical distance measurement between two targets on an image (detail).

Measurement results are listed in table 3.7, reporting values for each image and for both ultrasound devices.

Vertical distance		
Vertical distance between top of image and target at 2 cm depth		
	Butterfly iQ+	*Standard ultrasound system*
A_18_80	18.73 mm	18.77 mm
A_18_85	18.52 mm	18.51 mm
A_18_90	18.53 mm	18.54 mm
Vertical distance between targets at 2 cm and 4 cm depth		
	Butterfly iQ+	*Standard ultrasound system*

A_18_80	18.54 mm	19.12 mm
A_18_85	18.64 mm	18.75 mm
A_18_90	18.63 mm	18.60 mm
Vertical distance between targets at 4 cm and 6 cm depth		
	Butterfly iQ+	*Standard ultrasound system*
A_18_80	19.18 mm	19.63 mm
A_18_85	19.11 mm	19.42 mm
A_18_90	19.59 mm	19.28 mm
Vertical distance between targets at 6 cm and 8 cm depth		
	Butterfly iQ+	*Standard ultrasound system*
A_18_80	19.18 mm	19.75 mm
A_18_85	19.35 mm	19.75 mm
A_18_90	19.34 mm	19.47 mm
Vertical distance between targets at 8 cm and 10 cm depth		
	Butterfly iQ+	*Standard ultrasound system*
A_18_80	19.76 mm	19.89 mm
A_18_85	19.82 mm	19.94 mm
A_18_90	19.87 mm	19.80 mm
Vertical distance between targets at 10 cm and 12 cm depth		
	Butterfly iQ+	*Standard ultrasound system*
A_18_80	19.49 mm	19.49 mm
A_18_85	19.47 mm	19.65 mm
A_18_90	19.52 mm	19.83 mm
Vertical distance between targets at 12 cm and 14 cm depth		
	Butterfly iQ+	*Standard ultrasound system*
A_18_80	19.73 mm	19.97 mm
A_18_85	19.80 mm	20.00 mm
A_18_90	20.02 mm	19.85 mm
Vertical distance between targets at 14 cm and 16 cm depth		
	Butterfly iQ+	*Standard ultrasound system*
A_18_80	19.31 mm	19.80 mm
A_18_85	19.43 mm	19.77 mm
A_18_90	19.42 mm	19.75 mm

Table 3.7. Vertical distance measurement values.

At this point, mean and standard deviation have been computed over the measured values related to each group of images. In addition, deviations of each mean measurement from reference value (20 mm) have been calculated for each couple of targets, as listed in table 3.8. Measurement errors having negative values indicate measured distances that are smaller than the actual distances.

Vertical distance accuracy results
Vertical distance measurement between top of image and target at 2 cm depth

	Butterfly iQ+	*Standard ultrasound system*
Mean (mm)	18.59	18.61
SD (mm)	0.12	0.14
Error (mm)	-1.41	-1.39

Vertical distance measurement between targets at 2 cm and 4 cm depth

	Butterfly iQ+	*Standard ultrasound system*
Mean (mm)	18.60	18.82
SD (mm)	0.05	0.27
Error (mm)	-1.40	-1.18

Vertical distance measurement between targets at 4 cm and 6 cm depth

	Butterfly iQ+	*Standard ultrasound system*
Mean (mm)	19.29	19.44
SD (mm)	0.26	0.18
Error (mm)	-0.71	-0.56

Vertical distance measurement between targets at 6 cm and 8 cm depth

	Butterfly iQ+	*Standard ultrasound system*
Mean (mm)	19.29	19.66
SD (mm)	0.10	0.16
Error (mm)	-0.71	-0.34

Vertical distance measurement between targets at 8 cm and 10 cm depth

	Butterfly iQ+	*Standard ultrasound system*
Mean (mm)	19.82	19.88
SD (mm)	0.06	0.07
Error (mm)	-0.18	-0.12

Vertical distance measurement between targets at 10 cm and 12 cm depth

	Butterfly iQ+	*Standard ultrasound system*
Mean (mm)	19.49	19.66
SD (mm)	0.02	0.17
Error (mm)	-0.51	-0.34

Vertical distance measurement between targets at 12 cm and 14 cm depth

	Butterfly iQ+	*Standard ultrasound system*
Mean (mm)	19.85	19.94
SD (mm)	0.15	0.08
Error (mm)	-0.15	-0.06

Vertical distance measurement between targets at 14 cm and 16 cm depth

	Butterfly iQ+	*Standard ultrasound system*
Mean (mm)	19.39	19.78
SD (mm)	0.07	0.02
Error (mm)	-0.61	-0.22

Table 3.8. Vertical distance accuracy results.

Results of measurement errors are also illustrated in figure 3.9.

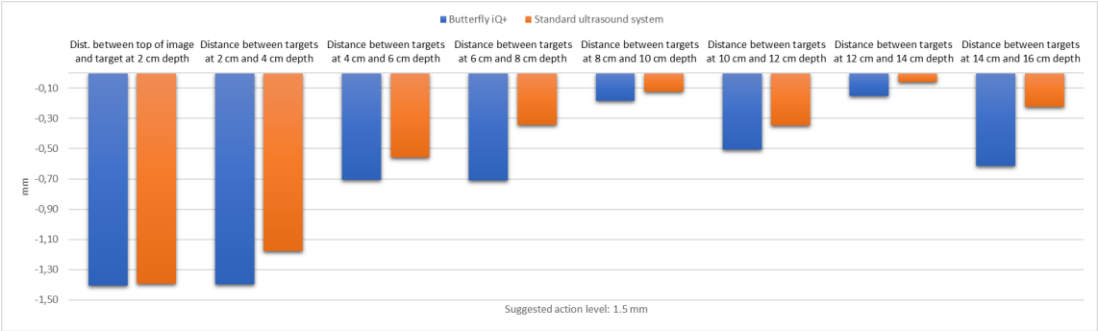

Figure 3.9. Vertical distance measurement errors.

It can be noticed that all errors committed for each couple of targets have negative value, and as already mentioned, it means that all measured distances are smaller than real distances. In particular, distance measurements of the most superficial targets are more affected by errors than measurements related to targets placed at greater depth. This is probably due to the fact that during the scan with the transducer, excessive pressure has been applied, temporarily compressing the targets and skewing the measurements. Nevertheless, even if Butterfly iQ+ commits errors greater than standard ultrasound system, both devices perform vertical distance measurements whose values are included into the accepted tolerance range.

Horizontal distance measurement

Phantom documentation specifies as reference value the horizontal distance between two consecutive targets, equal to *20 mm*. Action level suggested for this test corresponds to *2 mm*.

Combination of settings according to acquisition protocol has led to the acquisition of six images. Only aorta & gallbladder preset has been used, since horizontal group of targets in the phantom are located at 9 cm depth, and only a convex beam could explore targets at such depth. An example of measurement made on MATLAB between two adjacent horizontal targets is shown in figures 3.10 and 3.11.

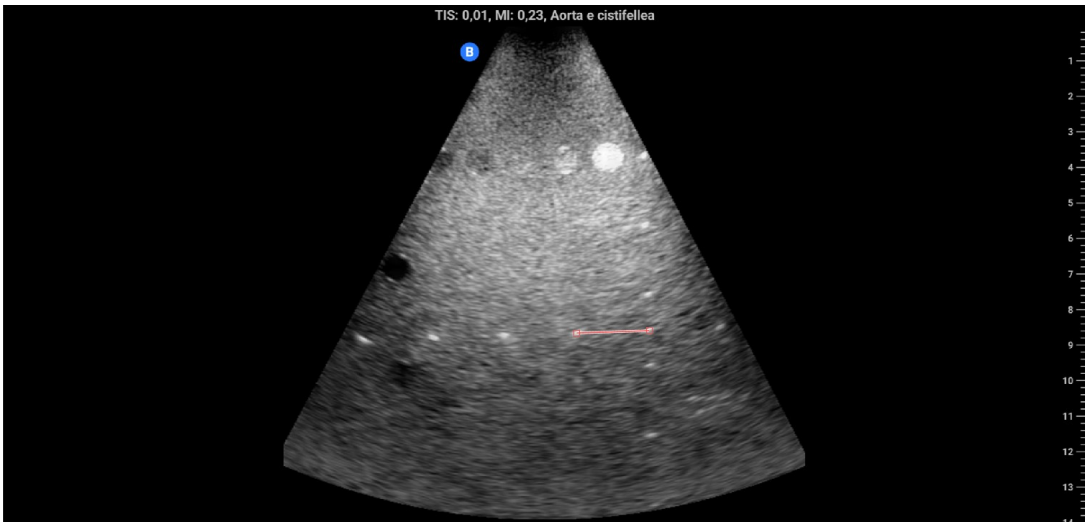

Figure 3.10. Example of horizontal distance measurement between two targets on an image.

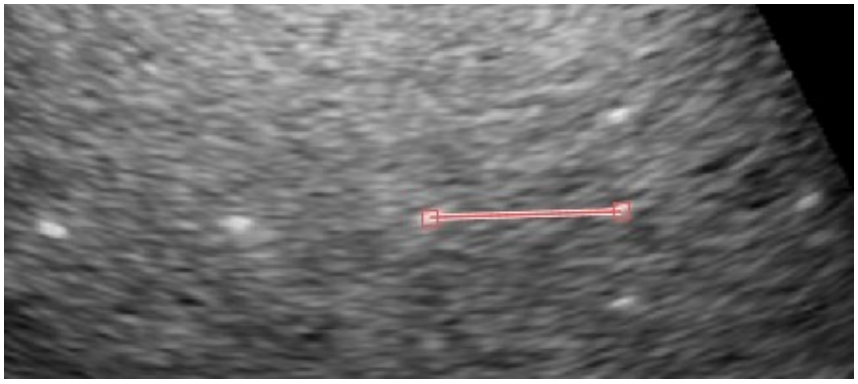

Figure 3.11. Example of horizontal distance measurement between two targets on an image (detail).

Measurement results are listed in table 3.9, reporting values for each image and for both ultrasound devices. Unlike standard ultrasound system, images generated by Butterfly iQ+ have a narrower field of view which has caused the impossibility to image all 7 targets in the same frame. For this reason, only first 6 horizontal targets are displayed in Butterfly iQ+, while measurement values provided by traditional ultrasound device and related to target 7 have been excluded from data analysis.

Horizontal distance		
Horizontal distance between targets 1 and 2		
	Butterfly iQ+	*Standard ultrasound system*
A_12_70	19.94 mm	19.59 mm
A_12_75	19.77 mm	20.18 mm
A_12_80	19.52 mm	19.78 mm
A_14_70	20.00 mm	19.44 mm
A_14_75	20.30 mm	19.55 mm
A_14_80	19.52 mm	19.79 mm
Horizontal distance between targets 2 and 3		
	Butterfly iQ+	*Standard ultrasound system*
A_12_70	19.82 mm	19.85 mm

A_12_75	19.93 mm	19.51 mm
A_12_80	19.57 mm	19.67 mm
A_14_70	19.73 mm	20.10 mm
A_14_75	20.22 mm	20.00 mm
A_14_80	20.01 mm	19.82 mm

Horizontal distance between targets 3 and 4

	Butterfly iQ+	*Standard ultrasound system*
A_12_70	20.13 mm	20.25 mm
A_12_75	20.05 mm	20.20 mm
A_12_80	20.21 mm	20.30 mm
A_14_70	20.86 mm	19.98 mm
A_14_75	19.96 mm	20.19 mm
A_14_80	20.44 mm	19.91 mm

Horizontal distance between targets 4 and 5

	Butterfly iQ+	*Standard ultrasound system*
A_12_70	20.30 mm	20.46 mm
A_12_75	20.46 mm	20.37 mm
A_12_80	20.17 mm	20.22 mm
A_14_70	20.17 mm	20.37 mm
A_14_75	20.53 mm	20.27 mm
A_14_80	20.05 mm	20.50 mm

Horizontal distance between targets 5 and 6

	Butterfly iQ+	*Standard ultrasound system*
A_12_70	19.75 mm	20.14 mm
A_12_75	19.61 mm	20.26 mm
A_12_80	20.12 mm	20.23 mm
A_14_70	20.08 mm	20.33 mm
A_14_75	20.12 mm	20.24 mm
A_14_80	20.33 mm	20.08 mm

Horizontal distance between targets 6 and 7

	Butterfly iQ+	*Standard ultrasound system*
A_12_70	*	19.42 mm
A_12_75	*	19.73 mm
A_12_80	*	19.71 mm
A_14_70	*	19.75 mm
A_14_75	*	19.71 mm
A_14_80	*	19.86 mm

* = value not available, target 7 not displayed

Table 3.9. Horizontal distance measurement values.

At this point, mean and standard deviation have been computed over the measured values related to each group of images. In addition, deviations of each mean measurement from reference value (20 mm) have been calculated for each couple of targets, as listed in table 3.10. Measurement

errors having negative values indicate measured distances that are smaller than the actual distances.

Horizontal distance accuracy results		
Horizontal distance measurement between targets 1 and 2		
	Butterfly iQ+	*Standard ultrasound system*
Mean (mm)	19.84	19.72
SD (mm)	0.30	0.26
Error (mm)	-0.16	-0.28
Horizontal distance measurement between targets 2 and 3		
	Butterfly iQ+	*Standard ultrasound system*
Mean (mm)	19.88	19.83
SD (mm)	0.23	0.22
Error (mm)	-0.12	-0.17
Horizontal distance measurement between targets 3 and 4		
	Butterfly iQ+	*Standard ultrasound system*
Mean (mm)	20.27	20.14
SD (mm)	0.33	0.16
Error (mm)	0.27	0.14
Horizontal distance measurement between targets 4 and 5		
	Butterfly iQ+	*Standard ultrasound system*
Mean (mm)	20.28	20.36
SD (mm)	0.19	0.11
Error (mm)	0.28	0.36
Horizontal distance measurement between targets 5 and 6		
	Butterfly iQ+	*Standard ultrasound system*
Mean (mm)	20.00	20.21
SD (mm)	0.27	0.09
Error (mm)	0.00	0.21
Horizontal distance measurement between targets 6 and 7		
	Butterfly iQ+	*Standard ultrasound system*
Mean (mm)	*	19.70
SD (mm)	*	0.15
Error (mm)	*	-0.30
* = value not available, target 7 not displayed		

Table 3.10. Horizontal distance accuracy results.

Results of measurement errors are also illustrated in figure 3.12, excluding values related to distance from target 7, since a comparison between the two devices is not possible in this case.

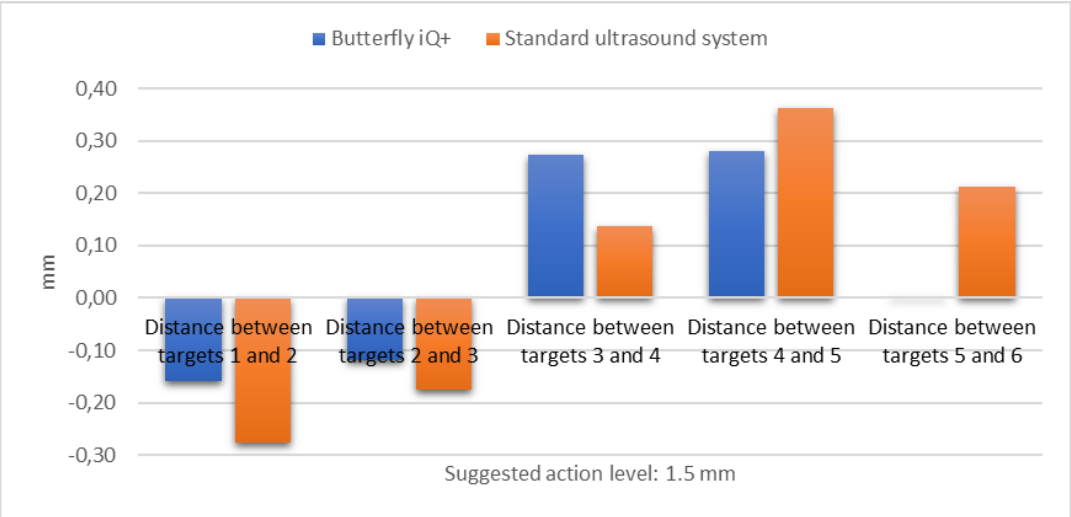

Figure 3.12. Horizontal distance measurement errors.

Results of horizontal distance measurements don't show any deviations larger than the estimated measurement accuracy, with all distance errors included into the suggested action levels.

Anechoic object imaging

To avoid geometric distortion and test the proper shape of anechoic structures, it has been considered as reference value an Aspect Ratio of *1*, which means that cylinders have the same height and width, equal to 8 mm according to the real diameter provided by phantom specifications in table **X**. Acceptance criterion considered for this test corresponds to the major geometric distortion accepted, that is *20%* of discrepancy from the ideal value of 1.

Combination of settings according to acquisition protocol has led to the acquisition of three images. Only aorta & gallbladder preset has been used, for the same reason as before, that is the possibility to image even deeper structures. An example of measurement made on MATLAB of height and width of one anechoic cylinder is shown in figures 3.13 and 3.14. Height and width respectively correspond to vertical and horizontal diameters, so the same MATLAB algorithm used for distance measurements has been exploited.

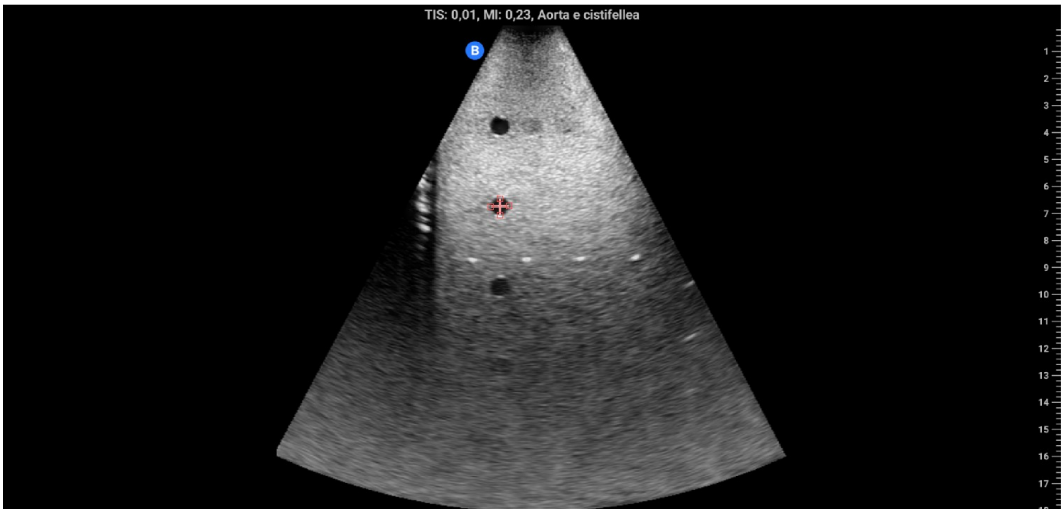

Figure 3.13. Example of horizontal and vertical diameters measurement on one anechoic cylinder on an image.

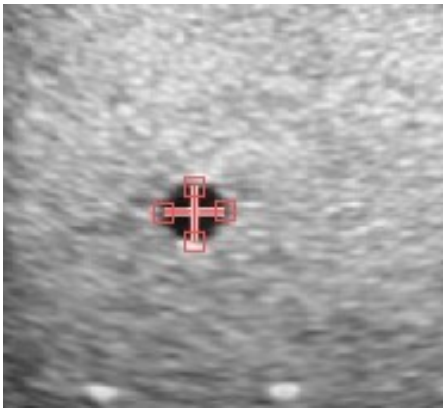

Figure 3.14. Example of horizontal and vertical diameters measurement on one anechoic cylinder on an image (detail).

After measurements of vertical and horizontal diameters, computation of Aspect Ratio for each cylinder has been realized, and results are listed in table 3.11, reporting values for each image and for both ultrasound devices. Unlike standard ultrasound system, images generated by Butterfly iQ+ couldn't display cylinder at 16 cm depth, because it is located deeper than maximum depth of penetration (DOP) and it is covered by electronic noise of the system, so diameter's measurements are not possible for this target.

Aspect Ratio of anechoic objects		
Cylinder at 4 cm depth		
	Butterfly iQ+	*Standard ultrasound system*
A_18_80	0.964	0.893
A_18_85	0.941	0.950
A_18_90	0.966	0.935
Cylinder at 7 cm depth		
	Butterfly iQ+	*Standard ultrasound system*
A_18_80	0.934	1.014
A_18_85	0.882	1.004

A_18_90	0.882	1.017
Cylinder at 10 cm depth		
	Butterfly iQ+	*Standard ultrasound system*
A_18_80	0.977	0.953
A_18_85	0.953	1.033
A_18_90	0.899	0.948
Cylinder at 13 cm depth		
	Butterfly iQ+	*Standard ultrasound system*
A_18_80	0.686	0.896
A_18_85	0.846	0.981
A_18_90	0.807	0.897
Cylinder at 16 cm depth		
	Butterfly iQ+	*Standard ultrasound system*
A_18_80	*	0.936
A_18_85	*	0.984
A_18_90	*	0.936
* = value not available, cylinder not visible		

Table 3.11. Aspect Ratios values for anechoic objects.

At this point, mean and standard deviation have been computed over the Aspect Ratio values related to each group of images. In addition, deviations of each mean measurement from reference value (Aspect Ratio=1) have been calculated for each cylinder, as listed in table 3.12. In this case, errors are represented in percentage, as suggested by acceptance criteria. Errors having negative values indicate Aspect Ratios smaller than 1, which means that cylinders have vertical diameter shorter than horizontal diameter.

Aspect Ratio accuracy results		
Cylinder at 4 cm depth		
	Butterfly iQ+	*Standard ultrasound system*
Mean	0.957	0.926
SD	0.014	0.029
Error (%)	-4.30	-7.37
Cylinder at 7 cm depth		
	Butterfly iQ+	*Standard ultrasound system*
Mean	0.899	1.012
SD	0.030	0.007
Error (%)	-10.07	1.19
Cylinder at 10 cm depth		
	Butterfly iQ+	*Standard ultrasound system*
Mean	0.943	0.978
SD	0.040	0.048
Error (%)	-5.70	-2.18

Cylinder at 13 cm depth		
	Butterfly iQ+	*Standard ultrasound system*
Mean	0.780	0.925
SD	0.084	0.049
Error (%)	-22.03	-7.53
Cylinder at 16 cm depth		
	Butterfly iQ+	*Standard ultrasound system*
Mean	*	0.952
SD	*	0.028
Error (%)	*	-4.80

* = value not available, cylinder not visible

Table 3.12. Aspect Ratio accuracy results.

Results of errors in percentage are also illustrated in figure 3.15, excluding values related to cylinder at 16 cm depth, since a comparison between the two devices is not possible in this case.

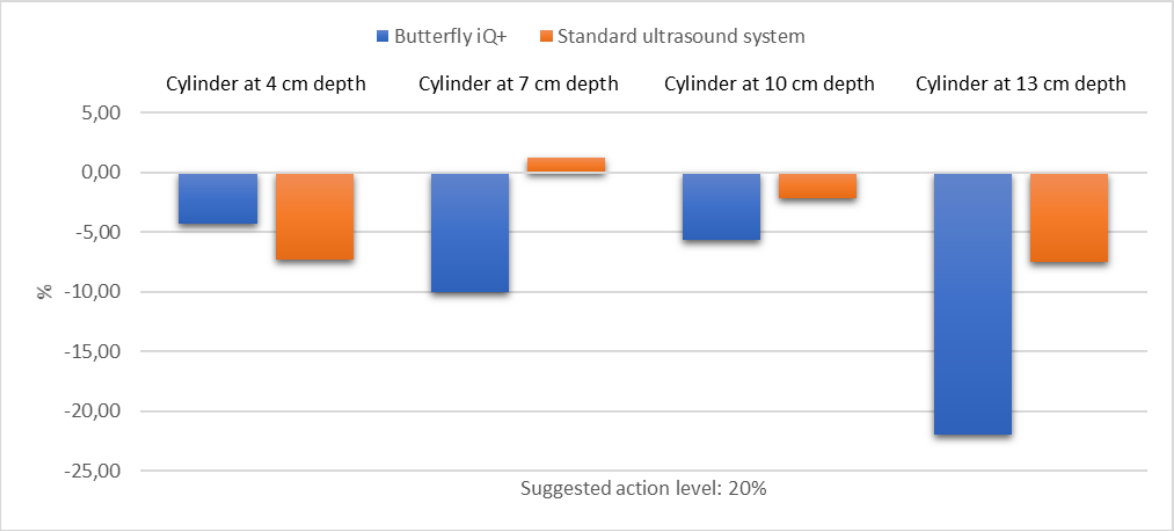

Figure 3.15. Major geometric distortion in terms of deviations from unitary Aspect Ratio.

Results of testing of the shape of anechoic structures by means of Aspect Ratio evaluation, show that geometric distortion of cylinders is included into the accepted tolerance limits, with the exception of the cylinder at 13 cm depth scanned by Butterfly iQ+ system, whose distortion causes a 22% of difference between its height and width. This slight excess of allowable distortion may be justified by the deep location of the anechoic objects, near the maximum depth of penetration for Butterfly iQ+ images, making targets barely visible at this depth and with less accurate measurements of their vertical and horizontal diameters.

Dead zone assessment

From now on, the following parameters tested do not have a specific reference value from which a certain accuracy is desirable, so only tolerance limits are provided. The goal of these tests is to check if measurement values are inside the action levels or not. For dead zone assessment, more than one action level is suggested depending on the transducer central frequency of the ultrasound system tested (as specified in table 3.3). Since Butterfly iQ+ system has a range of operating frequencies that can work from low to high frequencies, the most restrictive condition has been chosen as action level, and it corresponds to a dead zone distance equal to *3 mm*.

Combination of settings according to acquisition protocol has led to the acquisition of six images. Carotid and small organ presets have been used, since with their liner beam they are optimal for superficial imaging, as needed for this test. After the identification of the closest visible target among the near field group, it has been measured its distance from the scan surface. An example of measurement made on MATLAB of the dead zone distance is shown in figures 3.16 and 3.17.

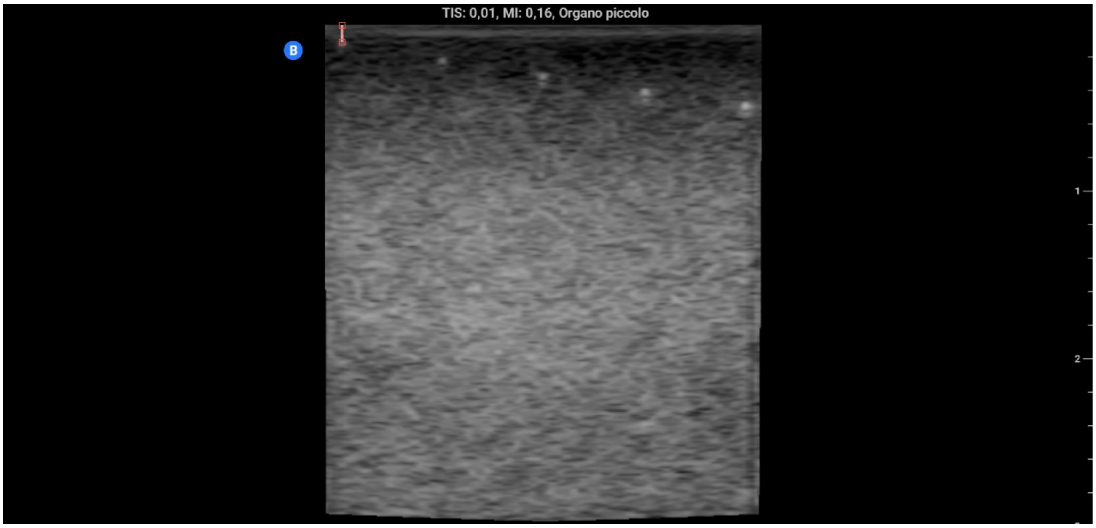

Figure 3.16. Example of dead zone distance measurement on an image.

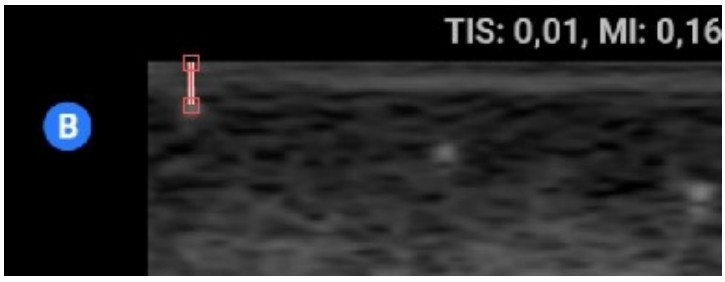

Figure 3.17. Example of dead zone distance measurement on an image (detail).

Measurement results are listed in table 3.13, reporting values for each image and for both ultrasound devices.

Dead zone assessment

	Butterfly iQ+	*Standard ultrasound system*
C_3_50	1.09 mm	1.59 mm
C_3_60	1.11 mm	1.47 mm
C_3_70	1.10 mm	1.52 mm
T_3_50	1.10 mm	1.57 mm
T_3_60	1.08 mm	1.57 mm
T_3_70	1.07 mm	1.68 mm

Table 3.13. Dead zone measurement values.

At this point, mean and standard deviation have been computed over the measured values related to all images, as listed in table 3.14 and represented in figure 3.18.

Dead zone results		
	Butterfly iQ+	*Standard ultrasound system*
Mean (mm)	1.09	1.57
SD (mm)	0.01	0.07

Table 3.14. Dead zone measurement results.

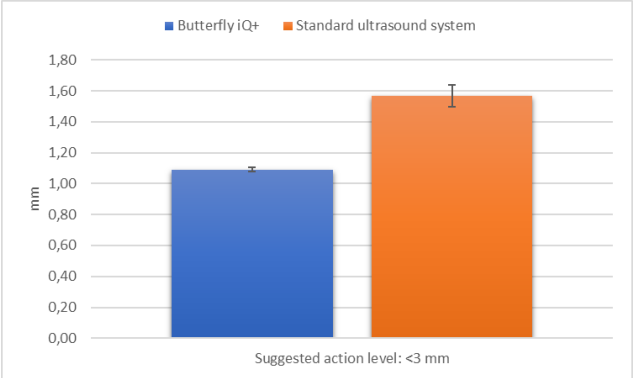

Figure 3.18. Dead zone measurement results.

For both devices, the nearest identifiable target was the wire filament located at 1 mm depth, therefore all dead zone distance measurements have met the acceptance criterion, resulting all distances from scan surface smaller than 3 mm.

Axial resolution

Action levels suggested for this test are equal to *1 mm* for high frequencies, corresponding to test made on the group of targets at 3 cm depth, and to *2 mm* for low frequencies, corresponding to the evaluation of axial resolution over the group of targets at 11 cm depth.

Combination of settings has led to the acquisition of twelve images for superficial targets and three images for deeper targets. Axial resolution has been estimated visually according to acquisition protocol, and an example of evaluation made over both groups of targets is illustrated in figures 3.19, 3.20, 3.21 and 3.22.

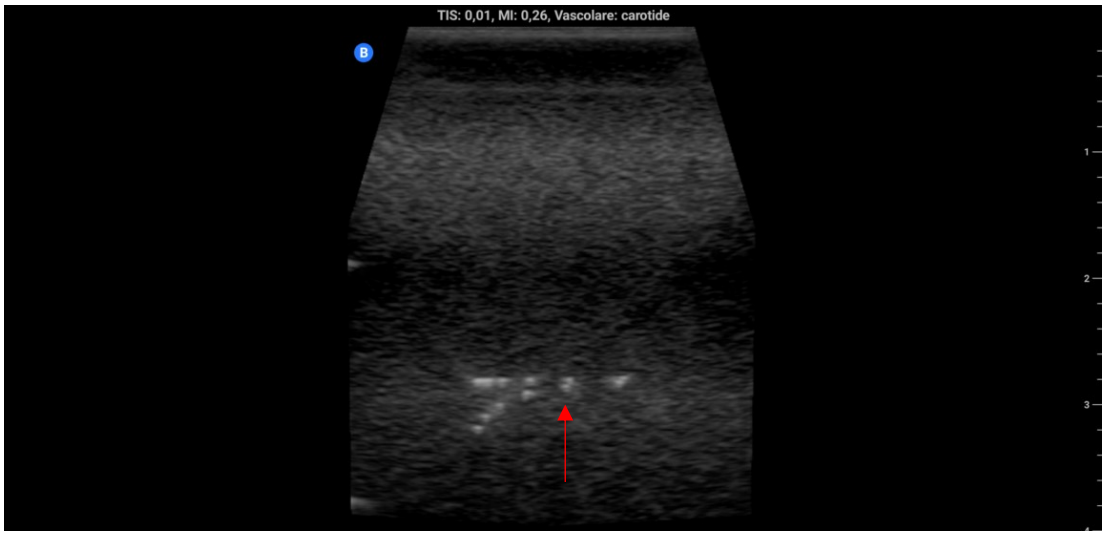

Figure 3.19. Example of axial resolution visual assessment on an image - targets at 3 cm depth.

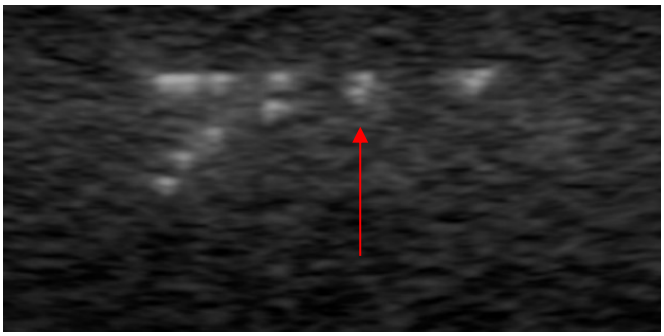

Figure 3.20. Example of axial resolution visual assessment on an image - targets at 3 cm depth (detail).

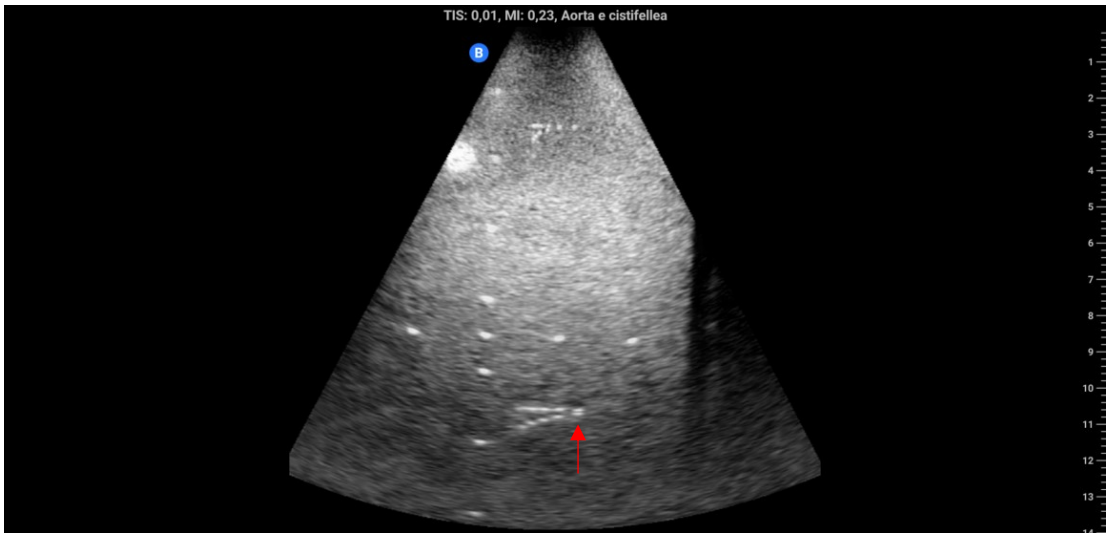

Figure 3.21. Example of axial resolution visual assessment on an image - targets at 11 cm depth.

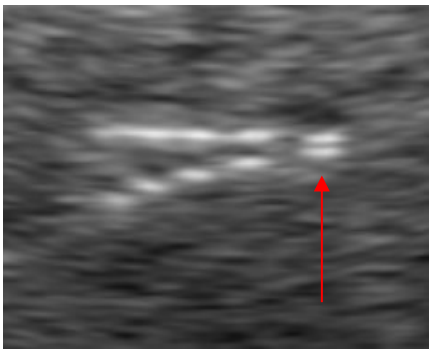

Figure 3.22. Example of axial resolution visual assessment on an image - targets at 11 cm depth (detail).

For both group of targets at different depths, the arrows point at the last two closely spaced targets that can be imaged separately along the axial direction, and the corresponding spacing between them according to tables 3.4 and 3.5 has been recorded as axial resolution. Results of all axial resolution assessments are listed in tables 3.15 and 3.16, reporting values for each image and for both ultrasound devices.

Axial resolution – targets at 3 cm depth		
	Butterfly iQ+	*Standard ultrasound system*
C_4_45	0.5 mm	0.25 mm
C_4_50	0.5 mm	0.25 mm
C_4_55	0.5 mm	0.25 mm
T_4_45	1 mm	0.5 mm
T_4_50	1 mm	0.5 mm
T_4_55	1 mm	0.5 mm
A_5_70	1 mm	1 mm
A_5_75	1 mm	1 mm
A_5_80	1 mm	1 mm
A_14_70	1 mm	1 mm
A_14_75	1 mm	1 mm
A_14_80	1 mm	1 mm

Table 3.15. Axial resolution values - targets at 3 cm depth.

Axial resolution – targets at 11 cm depth		
	Butterfly iQ+	*Standard ultrasound system*
A_14_70	1 mm	1 mm
A_14_75	1 mm	1 mm
A_14_80	1 mm	1 mm

Table 3.16. Axial resolution values - targets at 11 cm depth.

For both group of targets, mean and standard deviation have been computed over the axial resolution values related to all images, as listed in tables 3.17 and 3.18 and represented in figures 3.23 and 3.24.

Axial resolution results – targets at 3 cm depth		
	Butterfly iQ+	*Standard ultrasound system*
Mean (mm)	0.88	0.69
SD (mm)	0.23	0.34

Table 3.17. Axial resolution results – targets at 3 cm depth.

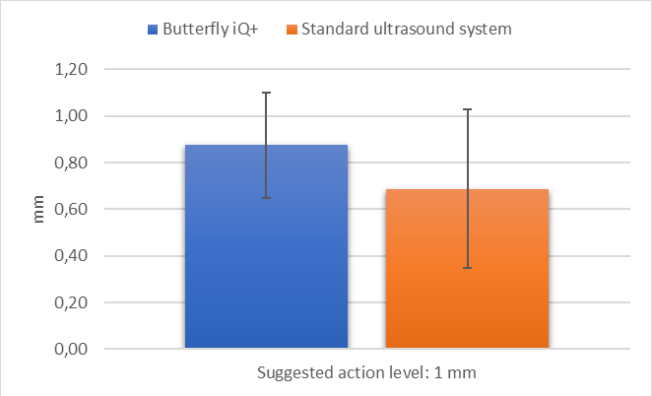

Figure 3.23. Axial resolution results - targets at 3 cm depth.

Axial resolution results – targets at 11 cm depth		
	Butterfly iQ+	*Standard ultrasound system*
Mean (mm)	1	1
SD (mm)	0	0

Table 3.18. Axial resolution results – targets at 11 cm depth.

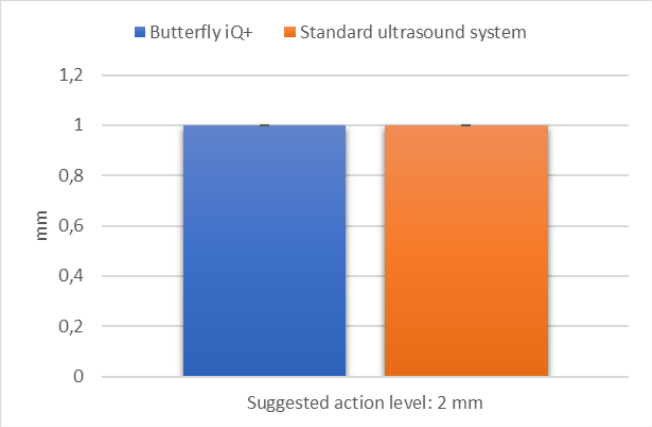

Figure 3.24. Axial resolution results – targets at 11 cm depth.

Results obtained show that axial resolution values are appropriate for both ultrasound systems and at both depth levels, staying under the suggested tolerance limits.

Lateral resolution

Action levels of lateral resolution suggested are equal to *1.5 mm* for the group of targets at 3 cm depth, and to *4 mm* for the group of targets at 11 cm depth.

Combination of settings has led to the acquisition of twelve images for superficial targets and three images for deeper targets, the same images used for the estimation of axial resolution. An example of evaluation made over both groups of targets is shown in figures 3.25, 3.26, 3.27 and 3.28.

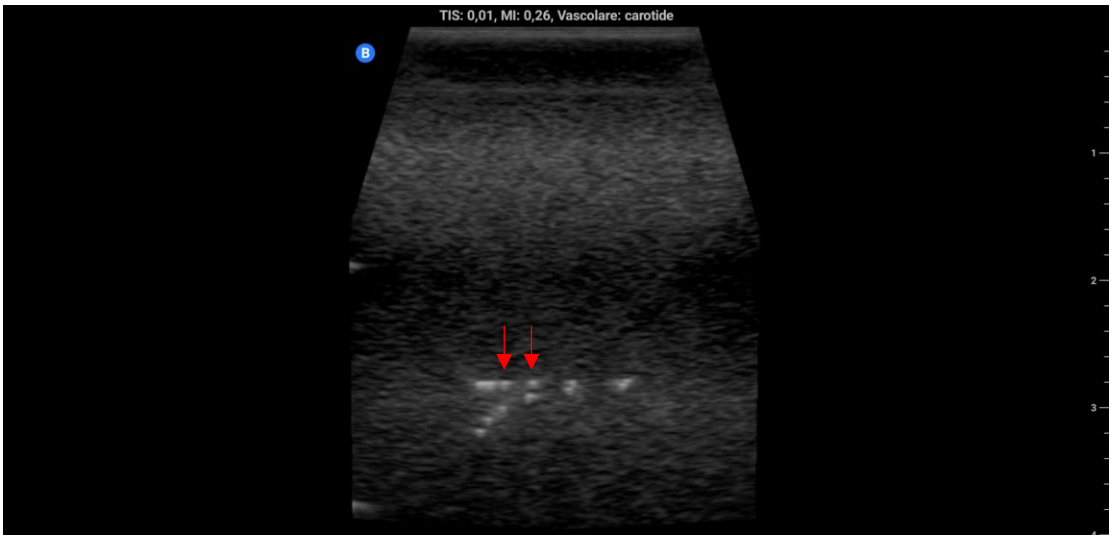

Figure 3.25. Example of lateral resolution visual assessment on an image - targets at 3 cm depth.

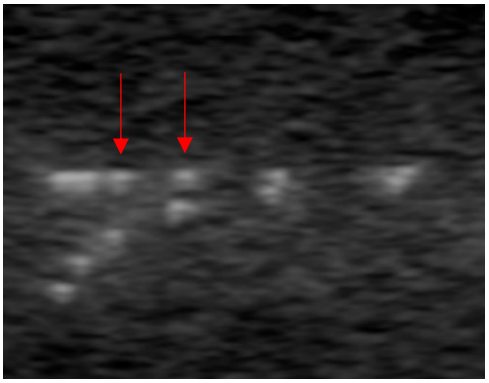

Figure 3.26. Example of lateral resolution visual assessment on an image - targets at 3 cm depth (detail).

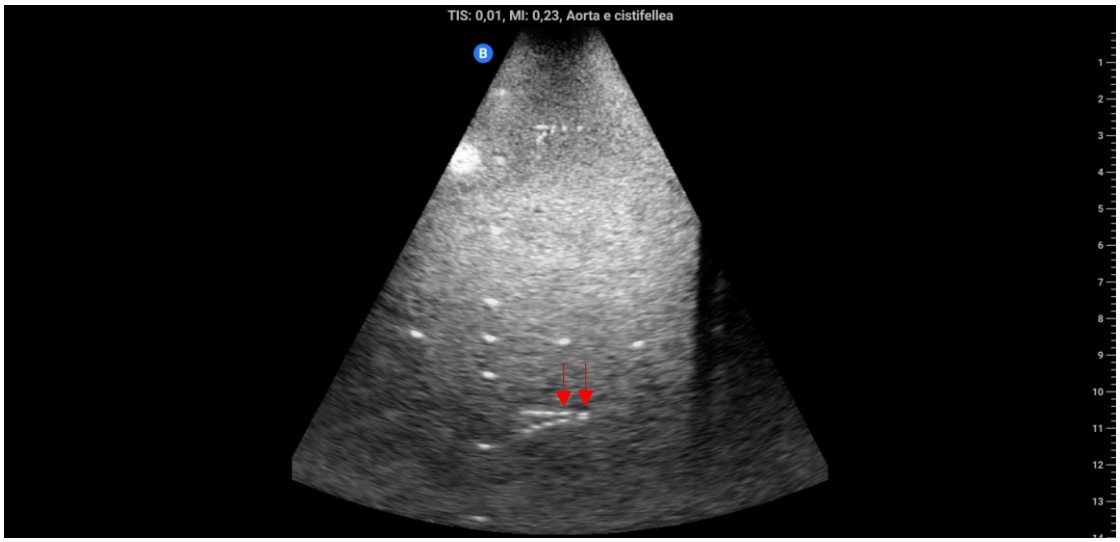

Figure 3.27. Example of lateral resolution visual assessment on an image - targets at 11 cm depth.

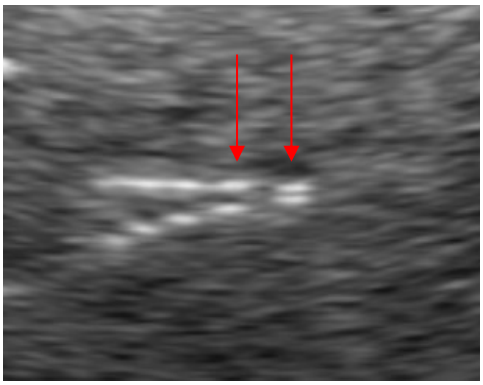

Figure 3.28. Example of lateral resolution visual assessment on an image - targets at 11 cm depth (detail).

For both group of targets at different depths, the arrows point at the last two closely spaced targets that can be imaged separately along the lateral direction, and the corresponding spacing between them according to tables 3.4 and 3.5 has been recorded as lateral resolution. Results of all lateral resolution assessments are listed in tables 3.19 and 3.20, reporting values for each image and for both ultrasound devices.

Lateral resolution – targets at 3 cm depth		
	Butterfly iQ+	*Standard ultrasound system*
C_4_45	2 mm	1 mm
C_4_50	2 mm	1 mm
C_4_55	2 mm	1 mm
T_4_45	1 mm	2 mm
T_4_50	1 mm	2 mm
T_4_55	1 mm	2 mm
A_5_70	2 mm	2 mm
A_5_75	2 mm	2 mm
A_5_80	2 mm	2 mm
A_14_70	2 mm	2 mm
A_14_75	2 mm	2 mm
A_14_80	2 mm	2 mm

Table 3.19. Lateral resolution values - targets at 3 cm depth.

Lateral resolution – targets at 11 cm depth		
	Butterfly iQ+	*Standard ultrasound system*
A_14_70	4 mm	3 mm
A_14_75	4 mm	4 mm
A_14_80	4 mm	3 mm

1table 3.20. Lateral resolution values - targets at 11 cm depth.

For both group of targets, mean and standard deviation have been computed over the lateral resolution values related to all images, as listed in tables 3.21 and 3.22 and represented in figures 3.29 and 3.30.

Lateral resolution results – targets at 3 cm depth		
	Butterfly iQ+	*Standard ultrasound system*
Mean (mm)	1.75	1.75

SD (mm)	0.45	0.45

Table 3.21. Lateral resolution results – targets at 3 cm depth.

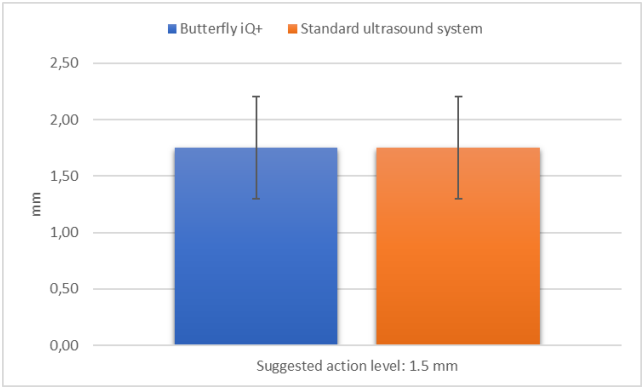

Figure 3.29. Lateral resolution results - targets at 3 cm depth.

Lateral resolution results – targets at 11 cm depth		
	Butterfly iQ+	*Standard ultrasound system*
Mean (mm)	4.00	3.33
SD (mm)	0.00	0.58

Table 3.22. Lateral resolution results – targets at 11 cm depth.

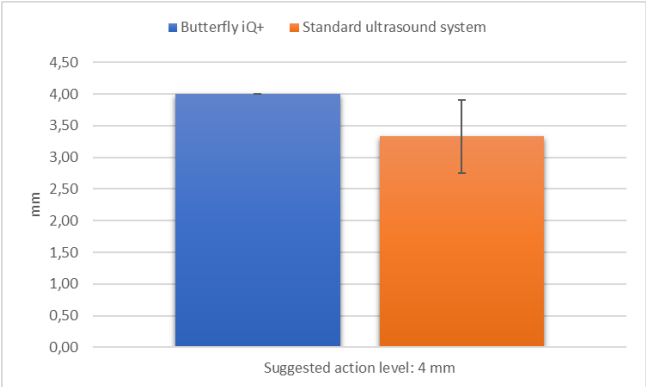

Figure 3.30. Lateral resolution results - targets at 11 cm depth.

Lateral resolution evaluated over target located at low depth on the images exceeds the accepted tolerance limits, and this is valid for both ultrasound system tested. On the contrary, lateral resolution results for deeper targets show appropriate values included inside the suggested action levels.

Image uniformity

Action level suggested for this test is *4 dB*. Combination of settings according to acquisition protocol has led to the acquisition of twenty-one images. An example of automatic selection of 4 ROIs on MATLAB for image uniformity assessment is reported in figure 3.31.

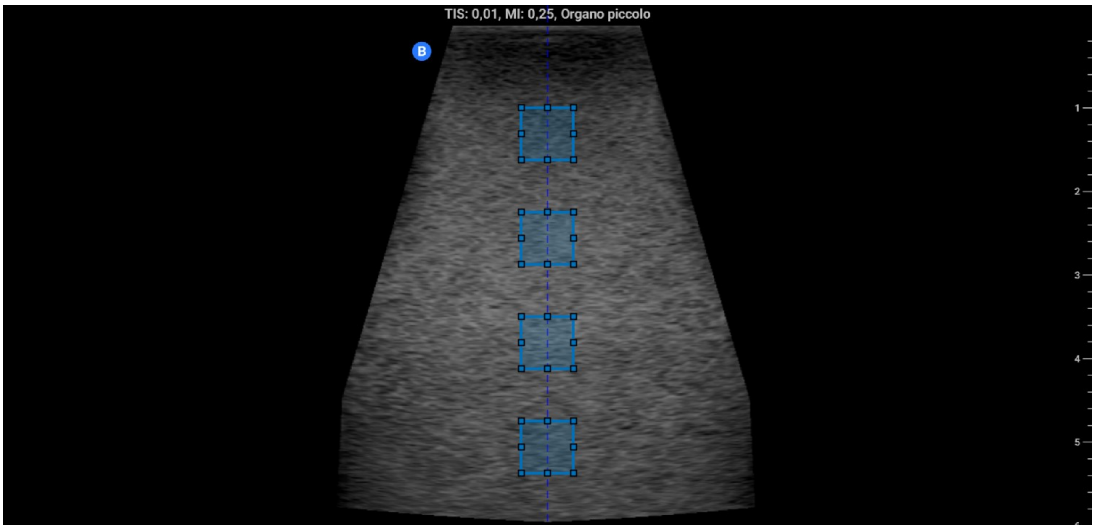

Figure 3.31. Example of automatic ROIs definition for image uniformity assessment.

Numeric results expressed in dB are listed in table 3.23, reporting values for each image and for both ultrasound systems.

Image uniformity		
	Butterfly iQ+	*Standard ultrasound system*
A_5_75	8.61 dB	3.95 dB
A_5_80	7.72 dB	0.64 dB
A_5_85	6.66 dB	2.62 dB
A_10_75	4.48 dB	2.84 dB
A_10_80	4.09 dB	2.67 dB
A_10_85	3.55 dB	2.11 dB
A_14_75	5.11 dB	7.24 dB
A_14_80	3.54 dB	5.33 dB
A_14_85	2.72 dB	4.91 dB
C_3_50	3.10 dB	1.10 dB
C_3_60	2.46 dB	0.73 dB
C_3_70	2.02 dB	0.44 dB
C_6_50	0.86 dB	2.19 dB
C_6_60	0.66 dB	0.58 dB
C_6_70	0.55 dB	0.32 dB
T_3_50	2.06 dB	1.76 dB
T_3_60	1.70 dB	1.07 dB
T_3_70	1.44 dB	0.71 dB
T_6_50	1.51 dB	1.96 dB
T_6_60	1.22 dB	0.32 dB
T_6_70	1.03 dB	0.24 dB

Table 3.23. Image uniformity values in dB.

Calculation of mean and standard deviation between uniformity values related to all images has led to the following results:

Image uniformity results	
Butterfly iQ+	*Standard ultrasound system*

Mean (dB)	3.10	2.08
SD (dB)	2.31	1.90

Table 3.24. Image uniformity results.

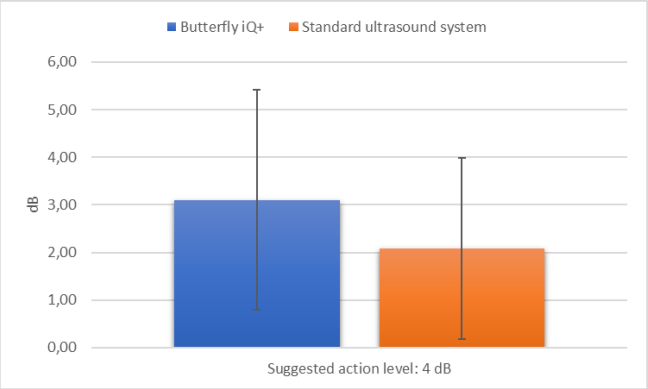

Figure 3.32. Image uniformity results.

Test results report that average uniformity values respect the tolerance limits, even if many values related to the single image exceed not only action levels, but also defect levels, justifying the high standard deviation in this case. Passing of tolerance limits occurs for both devices, but in a greater measure for Butterfly iQ+, and it can be also noticed that images acquired with aorta & gallbladder preset are those with the highest levels of nonuniformity.

Contrast response

Contrast response is the only image quality indicator tested in this study with no suggested tolerance limits, even if reference values are provided, and they are related to contrast nominal values in dB of gray scale targets, specified by phantom documentation. They range from anechoic (<-15 dB), to -6 dB, -3 dB, +3 dB, +6 dB, up to hyperechoic (>+15 dB). Combination of settings according to acquisition protocol has led to the acquisition of three images.

Unlike standard ultrasound system, images generated by Butterfly iQ+ have a narrower field of view, as already dealt in horizontal distance test results. This has caused the impossibility to image all six cylinders in the same frame. Therefore, cylinders have been separated in groups of three at a time, so each Butterfly iQ+ images display three targets instead of all six.

To calculate contrast with respect to background, an example of selection of two circular ROIs, one inside the target and the other one in the background, is shown in figure 3.33.

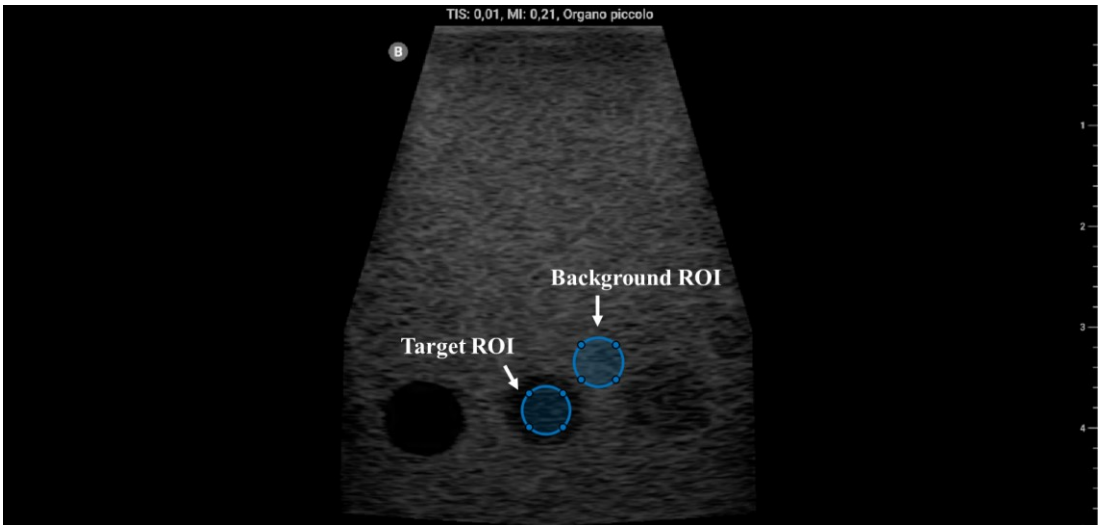

Figure 3.33. Example of selection of ROIs for contrast evaluation of one target with respect to background.

Results of contrast calculation for each echogenic cylinder and for each ultrasound system are listed in table 3.25.

Contrast response		
Anechoic cylinder (<-15 dB)		
	Butterfly iQ+	*Standard ultrasound system*
T_5_60	-33.35 dB	-7.49 dB
T_5_65	-22.64 dB	-5.68 dB
T_5_70	-23.16 dB	-4.24 dB
-6 dB cylinder		
	Butterfly iQ+	*Standard ultrasound system*
T_5_60	-5.63 dB	-2.41 dB
T_5_65	-4.51 dB	-0.93 dB
T_5_70	-3.83 dB	-0.74 dB
-3 dB cylinder		
	Butterfly iQ+	*Standard ultrasound system*
T_5_60	-3.50 dB	-1.12 dB
T_5_65	-2.98 dB	-0.36 dB
T_5_70	-2.76 dB	-0.26 dB
+3 dB cylinder		
	Butterfly iQ+	*Standard ultrasound system*
T_5_60	1.91 dB	3.18 dB
T_5_65	1.49 dB	0.11 dB
T_5_70	1.06 dB	0.11 dB
+6 dB cylinder		
	Butterfly iQ+	*Standard ultrasound system*
T_5_60	2.88 dB	3.23 dB
T_5_65	3.05 dB	0.62 dB
T_5_70	2.31 dB	0.52 dB

Hyperechoic cylinder (>+15 dB)		
	Butterfly iQ+	*Standard ultrasound system*
T_5_60	7.60 dB	4.64 dB
T_5_65	7.08 dB	2.95 dB
T_5_70	5.91 dB	2.10 dB

Table 3.25. Contrast values in dB.

Calculation of mean and standard deviation between contrast values related to all images has led to the results listed in table 3.26, and also measurement accuracy has been evaluated in terms of average contrast deviation from nominal values.

Contrast results		
Anechoic cylinder (<-15 dB)		
	Butterfly iQ+	*Standard ultrasound system*
Mean (dB)	-26.38	-5.81
SD (dB)	6.04	1.63
Error (dB)	-11.38	9.19
-6 dB cylinder		
	Butterfly iQ+	*Standard ultrasound system*
Mean (dB)	-4.65	-1.36
SD (dB)	0.91	0.92
Error (dB)	1.35	4.64
-3 dB cylinder		
	Butterfly iQ+	*Standard ultrasound system*
Mean (dB)	-3.08	-0.58
SD (dB)	0.38	0.47
Error (dB)	-0.08	2.42
+3 dB cylinder		
	Butterfly iQ+	*Standard ultrasound system*
Mean (dB)	1.49	1.14
SD (dB)	0.42	1.77
Error (dB)	-1.51	-1.86
+6 dB cylinder		
	Butterfly iQ+	*Standard ultrasound system*
Mean (dB)	2.75	1.46
SD (dB)	0.39	1.53
Error (dB)	-3.25	-4.54
Hyperechoic cylinder (>+15 dB)		
	Butterfly iQ+	*Standard ultrasound system*
Mean (dB)	6.86	3.23
SD (dB)	0.87	1.29
Error (dB)	-8.14	-11.77

Table 3.26. Contrast results.

Results of deviations from reference values are also illustrated in figure 3.34.

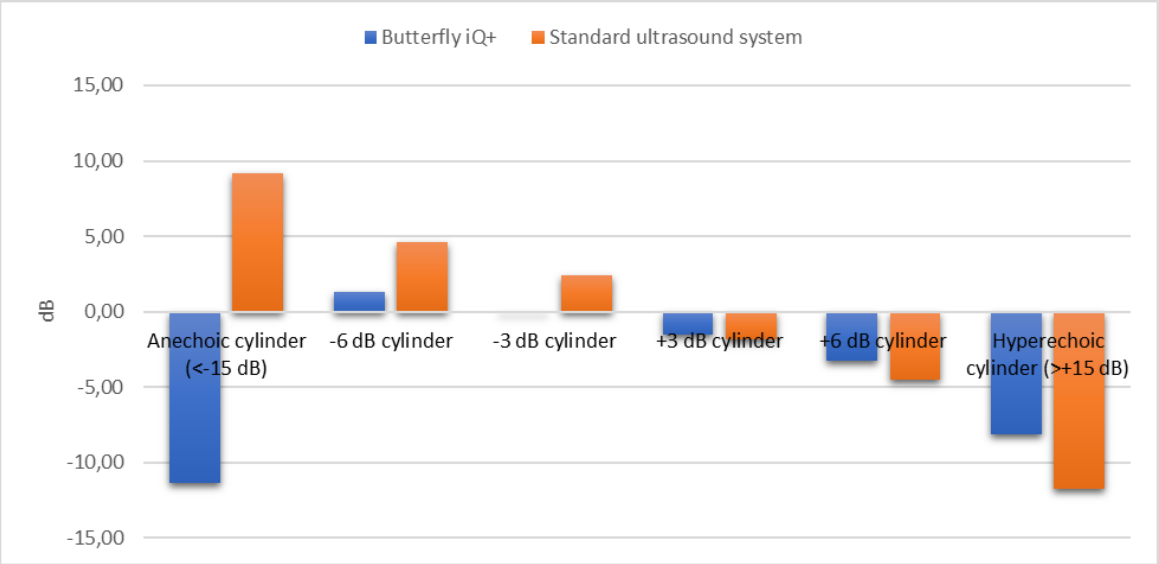

Figure 3.34. Contrast errors.

For negative contrast targets, a positive error means that they actually produce less contrast than expected, while for positive contrast targets, results show that their real contrast is lower than expected through a negative error. Therefore, for all targets there is an overall weak contrast with respect to background. Negative error for anechoic cylinder produced by Butterfly iQ+ images must not be taken in account, since reference value for that target indicates a desirable contrast minor than -15 dB and not exactly equal to that specific value, and since results show much more contrast than expected, that error does not represent a real deviation from reference value. As already mentioned, these contrast values may be considered as the new baseline values for future tests.

3.4.4 Paired-sample t-test

After the evaluation of measurement accuracy for Butterfly iQ+ system and for traditional ultrasound machine, performed comparing results with respect to reference values, an additional analysis has been carried out, in particular a paired-sample t-test has been conducted, to compare the measurement differences between the two systems.

This statistical procedure determines whether the mean difference between two sets of observations – results of the tests performed by two ultrasound systems in this case – is zero. Statistical results return a test decision for the null hypothesis, assuming that the true difference between the paired samples comes from a normal distribution with mean equal to zero. The alternative hypothesis is that the population distribution does not have a mean equal to zero. Result is 1 if the test rejects the null hypothesis, and 0 otherwise.

A 95% confidence level has been used in this statistical testing, so if the p-value is greater than 0.05 and null hypothesis is not rejected, results obtained by Butterfly iQ+ system and those from standard ultrasound machine are judged statistically the same, which means that their performances on image quality tests are very comparable. Under this model, all observable differences are explained by random variations. Conversely, statistical significance has been considered if $p<0.05$ and null hypothesis is rejected, and this is an undesired condition since after proving that not only Butterfly iQ+ sometimes commits measurement errors from reference values, it is desirable that at least errors from both systems tested are comparable.

In the following tables all paired-sample t-test results are listed. Sets of observations related to horizontal distance between targets 6 and 7, and aspect ratio of cylinders at 16 cm depth have been excluded from the statistical analysis, since one of the two samples was not available due to targets not displayed or targets not visible. P-values with *, ** and *** are indicating statistical significances $p<0.05$, $p<0.01$ and $p<0.001$, respectively.

Paired-sample t-test results for vertical distance measurements

Vertical distance between top of image and target at 2 cm depth

p-value	*Test decision for the null hypothesis*
0.4557	0

Vertical distance between targets at 2 cm and 4 cm depth

p-value	*Test decision for the null hypothesis*
0.3554	0

Vertical distance between targets at 4 cm and 6 cm depth

p-value	*Test decision for the null hypothesis*
0.5865	0

Vertical distance between targets at 6 cm and 8 cm depth

p-value	*Test decision for the null hypothesis*
0.1035	0

Vertical distance between targets at 8 cm and 10 cm depth

p-value	*Test decision for the null hypothesis*
0.4538	0

Vertical distance between targets at 10 cm and 12 cm depth

p-value	*Test decision for the null hypothesis*
0.2108	0

Vertical distance between targets at 12 cm and 14 cm depth

p-value	*Test decision for the null hypothesis*
0.5617	0

Vertical distance between targets at 14 cm and 16 cm depth

p-value	*Test decision for the null hypothesis*	
0.0174	1	→ p<0.05*

Table 3.27. Vertical distance statistical analysis.

Paired-sample t-test results for horizontal distance measurements	
Horizontal distance between targets 1 and 2	
p-value	*Test decision for the null hypothesis*
0.5778	0
Horizontal distance between targets 2 and 3	
p-value	*Test decision for the null hypothesis*
0.6501	0
Horizontal distance between targets 3 and 4	
p-value	*Test decision for the null hypothesis*
0.4961	0
Horizontal distance between targets 4 and 5	
p-value	*Test decision for the null hypothesis*
0.4362	0
Horizontal distance between targets 5 and 6	
p-value	*Test decision for the null hypothesis*
0.1471	0

Table 3.28. Horizontal distance statistical analysis.

Paired-sample t-test results for anechoic objects imaging		
Cylinder at 4 cm depth		
p-value	*Test decision for the null hypothesis*	
0.3116	0	
Cylinder at 7 cm depth		
p-value	*Test decision for the null hypothesis*	
0.0211	1	→ p<0.05*
Cylinder at 10 cm depth		
p-value	*Test decision for the null hypothesis*	
0.3740	0	
Cylinder at 13 cm depth		
p-value	*Test decision for the null hypothesis*	
0.0536	0	

Table 3.29. Anechoic objects imaging statistical analysis.

Paired-sample t-test results for dead zone assessment	
p-value	*Test decision for the null hypothesis*

$3.5400 \cdot 10^{-5}$	1	→ p<0.001***

Table 3.30. Dead zone statistical analysis.

Paired-sample t-test results for axial resolution		
Targets at 3 cm depth		
p-value	*Test decision for the null hypothesis*	
0.0121	1	→ p<0.05*
Targets at 11 cm depth		
p-value	*Test decision for the null hypothesis*	
0.5865	0	

Table 3.31. Axial resolution statistical analysis.

Paired-sample t-test results for lateral resolution		
Targets at 3 cm depth		
p-value	*Test decision for the null hypothesis*	
1	0	
Targets at 11 cm depth		
p-value	*Test decision for the null hypothesis*	
0.1835	0	

Table 3.32. Lateral resolution statistical analysis.

Paired-sample t-test results for image uniformity		
p-value	*Test decision for the null hypothesis*	
0.0499	1	→ p<0.05*

Table 3.33. Image uniformity statistical analysis.

Paired-sample t-test results for contrast response		
Anechoic cylinder (<-15 dB)		
p-value	*Test decision for the null hypothesis*	
0.0168	1	→ p<0.05*
-6 dB cylinder		
p-value	*Test decision for the null hypothesis*	
0.0020	1	→ p<0.01**
-3 dB cylinder		
p-value	*Test decision for the null hypothesis*	
$7.6712 \cdot 10^{-4}$	1	→ p<0.001***
+3 dB cylinder		
p-value	*Test decision for the null hypothesis*	
0.7089	0	

+6 dB cylinder		
p-value	*Test decision for the null hypothesis*	
0.2646	0	
Hyperechoic cylinder (>+15 dB)		
p-value	*Test decision for the null hypothesis*	
0.0091	1	→ p<0.01**

Table 3.34. Contrast response statistical analysis.

Results demonstrated that over 29 possible comparisons between Butterfly iQ+ and standard ultrasound system, only 9 provide statistical significance and reject the null hypothesis. In particular, for vertical and horizontal distance measurements, the performance of Butterfly iQ+ system is comparable ($p>0.05$) to that of traditional ultrasound system, except for one single test made on a couple of vertical targets. Results of anechoic objects imaging provided by Butterfly iQ+ are comparable ($p>0.05$) to that of traditional ultrasound system for 3 tested targets of 4. Similar trend of anechoic objects imaging has been observed for axial and lateral resolution: there is significant difference ($p<0.05$) only for one axial resolution test made on superficial targets, while the other tests demonstrated similar performances. For dead zone assessment, Butterfly iQ+ show significantly ($p<0.001$) lower dead zone distance than standard ultrasound system. Image uniformity comparison has revealed a significance value of 0.0499, or $p<0.05$, which means that there is a slight statistical significance. Lastly, contrast response comparison between Butterfly iQ+ and standard ultrasound system has provided to the worst results: only 2 contrast tests of 6 (those made on +3 dB and +6 dB cylinders) demonstrate no significant differences and provide comparable results, while the other 4 tests show statistical significance and reject the null hypothesis.

3.5 Conclusions

Results obtained from the quantitative evaluation of image quality parameters have shown that, for certain tests, accuracy from reference value is not always observed. Sometimes both Butterfly iQ+ and standard ultrasound system commit errors that exceed the recommended tolerance limits. For this reason, a paired-value t-test has been conducted, to analyze if at least performances of both devices could be considered congruent or not.

From all these evaluations it is possible to conclude that: all tests involving distance measurements, that are vertical and horizontal distance measurements, anechoic object imaging and dead zone assessment, provide very good results: measurement accuracy is almost always respected, and even if Butterfly iQ+ in general commits errors greater than standard ultrasound system, their performances are statistically congruent. This latter consideration is not valid for

dead zone test though: differences between the two devices are highly statistically significant, but results of this test are still considered good since their errors remain under the recommended action levels. This observation is also valid for axial resolution test: one of two results of paired t-test shows statistical significance, but their values are all included into tolerance limits, so good results are obtained also for this image quality indicator.

Other tests, such as lateral resolution and image uniformity, provide results worse than those above mentioned. In particular, Butterfly iQ+ values of lateral resolution are statistically congruent with standard system results, but one of the two tests (performed on the superficial targets) exceeds the allowed threshold. Image uniformity test instead, provides results slightly statistically significant and in addition the distribution of values of nonuniformity is highly dispersive.

Lastly, worst results are obtained by contrast response: results are very distant from nominal contrast values and cannot even be considered statistically congruent with performances of conventional ultrasound equipment.

However, before concluding that Butterfly iQ+ performances are insufficient in terms of image quality and in particular for some specific parameter, contrast response above all, it is important to outline that there is the possibility that these errors may be attributed to other factors rather than real devices' performances. For example, an insufficient accuracy may be caused by variability in the markers' placement with cursor, when making the measurements directly on images on MATLAB. Another possible error source can be attributed to the intra-operator variability, that occurs when the same operator performs the acquisitions by scanning the phantom with both transducers. In fact, the repetition of these acquisitions over time can give more variable results, because of the different operator's pressing down on the phantom while performing the scans or the probe inclination, that can produce relevant changes on the repeated images. An additional parameter that could lead to errors, even if it has been demonstrated that tests involving distance measurements produce very accurate results, is the calibration factor evaluation for Butterfly iQ+ images, since it has been manually assessed, differently from conventional ultrasound equipment images whose DICOM format already provides this pixel-to-mm conversion factor.

Chapter 4

Butterfly iQ+ clinical applications

4.1 Introduction

The connection between engineering and clinical evaluation is fundamental to define that a certain device can be considered well-performing. In the previous chapter phantom images acquired with Butterfly iQ+ have been analysed, by means of quantitative evaluation of some parameters related to image quality. Although certain parameters tested did not prove to be optimal, it is however important to consider the effective uses that such device can have in clinical practice, and if the unperfect image quality can somehow represent an advantage in the doctors 'ability to provide appropriate diagnosis.

Regarding Butterfly iQ+ device, despite its ultrasound image quality results slightly inferior to that of a traditional ultrasound system, it still produces images that clinicians consider perfectly adequate to perform an ultrasonographic practice called Point-of-care ultrasound (POCUS). POCUS refers to the practice used by physicians to perform ultrasound scans and make diagnosis wherever the patient is being treated, whether that's at home, an ambulance, in an hospital, or a remote village. It is an immediate and quick ultrasound exam that allows medical professionals to get immediate answers from simple questions (such as yes/no, or present/absent), complementing a correct anamnesis and the physical examination. Therefore, it is used to perform a first-level differential diagnosis that could help to better understand patients, to make definitive diagnosis and avoid further second-level examinations resulting in cost saving, or to make diagnostic suspicions to be confirmed with a second-level diagnosis, including traditional ultrasound exam or other advanced imaging techniques (PET, CT, MRI, etc.).

For these reasons, POCUS should not be confused with a complete ultrasound exam, which is done by specialized radiologists through traditional ultrasound machines and provides a more

accurate investigation by evaluating the anatomy, the physiology and the potential pathology of a patient. POCUS instead focuses on specific questions that physicians ask to themselves according to the medical case under examination, and on decisions taken consequently to the answers.

Butterfly iQ+ probe is perfectly suitable for POCUS method: thanks to its portability, it is possible to visit patients directly on the point of care; its cloud storage allows to share ultrasound data and ask for a remote, real-time feedback to medical colleagues; moreover thanks to its versatility and its capability to perform whole-body imaging, it can be used in all emergency settings like ambulances or emergency rooms, but also in all outpatient clinics.

One of the main critical aspects of POCUS, also recurring in the majority of diagnostic techniques, is the operator variability: results of ultrasound examination affect physician's decision about the proper treatment, therefore such results must be reliable. For this reason, a correct education and training in the various applications of POCUS is fundamental for physicians. They must acquire fundamental skills like the knowledge of basic principles of ultrasound, the ability to correctly acquire ultrasound images, and the ability to read and interpret normal images and distinguish them from abnormal images. In addition to a proper technical and professional training for physicians, they must know the ultrasound system in use and must be aware of what they can expect from that device: they ask for ease of use in terms of ergonomics and immediate setting changes before performing a scan, the maintenance of visual attention avoiding fatigue due to the prolonged interaction with ultrasound screen, and the awareness that such device provides certain results.

4.2 Clinical image evaluation

To prove Butterfly iQ+ efficacy within the scope of POCUS, ultrasound images of various organs acquired with both Butterfly iQ+ and a standard ultrasound machine have been compared. The purpose of comparing images acquired in clinical environment is to verify if, although some parameters related to image quality are insufficient from a quantitative point of view, at least through a qualitative evaluation there is an overlap between images acquired by both devices. It is enough that images can be evaluated congruent from a qualitative point of view in clinical applications to consider Butterfly iQ+ adapt to be used for POCUS. Butterfly iQ+ may not have the same performances of a standard ultrasound machines in terms of technical parameters like contrast and resolution for example, but it's the use itself of the two devices to be different.

This study has been conducted in collaboration with Dr. R. Bertucci. Sixteen subjects, 6 females and 10 males with age between 27 and 62 years old, have been recruited for the acquisition of

ultrasound images related to various body organs, from thyroid to abdominal organs. Traditional ultrasound machine used for comparison is MyLab X8 (Esaote S.p.A., Genoa, Italy; L 4-15 and C 1-8 probes). Patient data have been collected for didactic purpose only and the subjects' privacy has been observed. Some examples of images of various organs in normal conditions acquired for comparison between the two devices are reported below.

4.2.1 Case 1

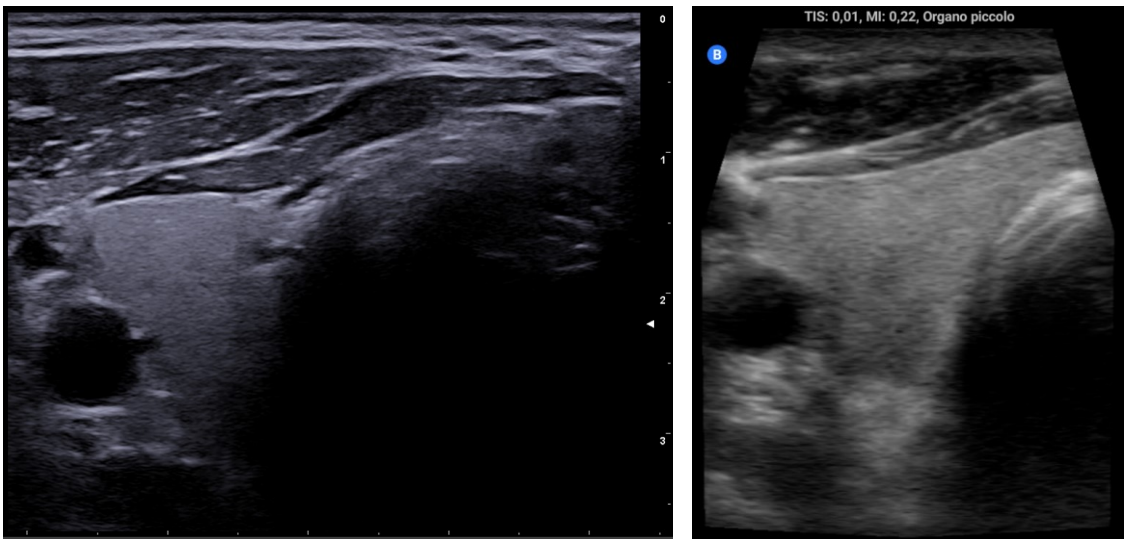

Figure 4.1. Thyroid ultrasound. Images from standard ultrasound machine (left) and from Butterfly iQ+ (right).

Figure 4.1 is an example of thyroid ultrasound, transverse scan of the right lobe. In the two images acquired by both ultrasound systems it is possible to identify the anterior thyroid profile, the profile attached to the trachea, the gland structure, the various layers of thyroid muscles, and the well-defined nearby vessels.

4.2.2 Case 2

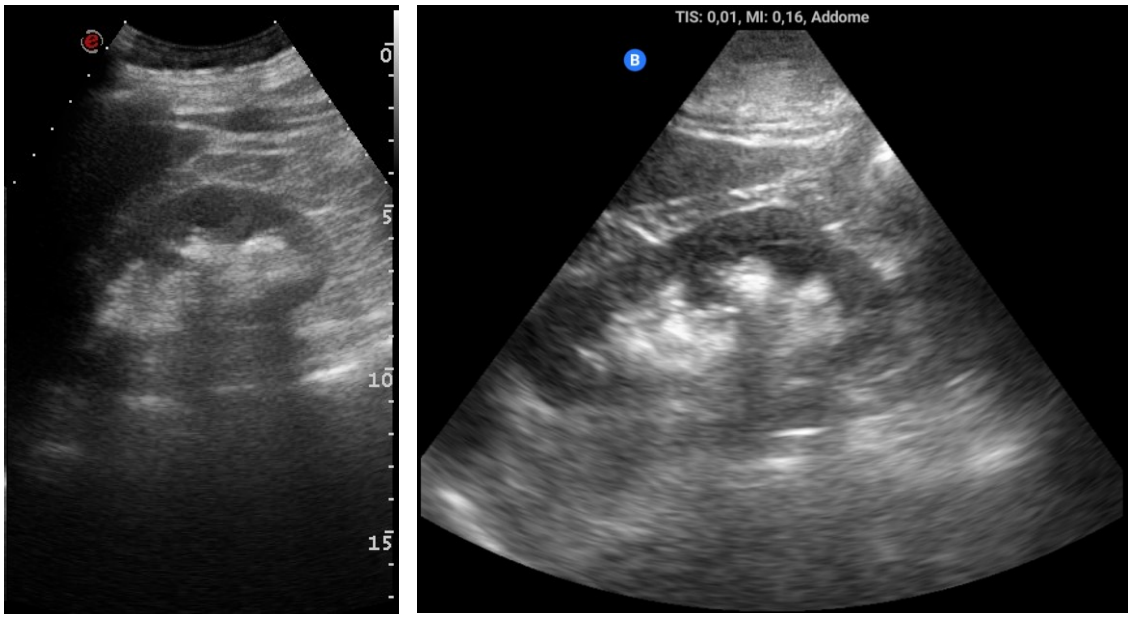

Figure 4.2. Kidney ultrasound. Images from standard ultrasound machine (left) and from Butterfly iQ+ (right).

Example of kidney ultrasound in longitudinal scan plane is shown in figure 4.2. Renal morphology is respected, and its dimensions too: the corticomedullary thickness is recognisable in both images. Renal capsular profile is well evident, and perirenal and pararenal tissues and renal pelvis stroma are definable. In both cases is evident the hyperechogenic formation, that is a kidney stone, that produces an acoustic shadow artifact.

4.2.3 Case 3

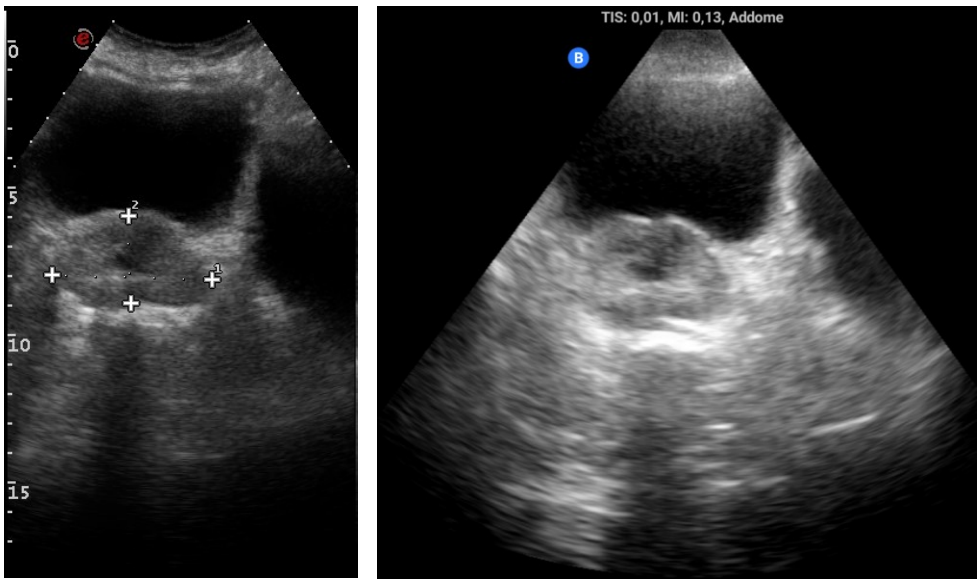

Figure 4.3. Suprapubic bladder and prostate ultrasound, transversal scan. Images from standard ultrasound machine (left) and from Butterfly iQ+ (right).

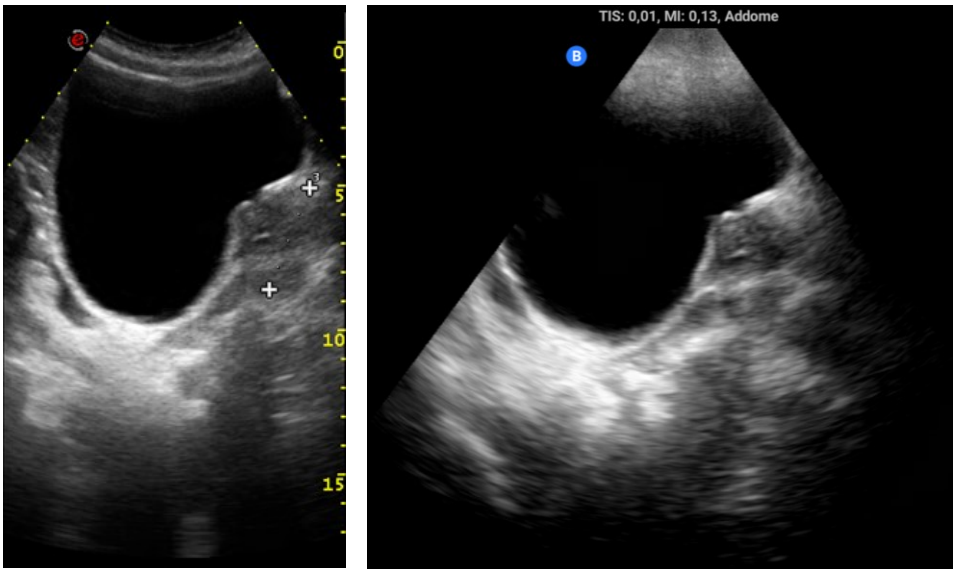

Figure 4.4. Suprapubic bladder and prostate ultrasound, longitudinal scan. Images from standard ultrasound machine (left) and from Butterfly iQ+ (right).

Figures 4.3 and 4.4 are an example of suprapubic bladder and prostate ultrasound in transversal and longitudinal scan planes. It is possible to easily evaluate the prostate profile (P) and its structure with its central hypoechoic area, but also the bladder wall (V), although images acquired with Butterfly iQ+ system could have been optimized with TCG adjustments in the top portion of images.

4.2.4 Case 4

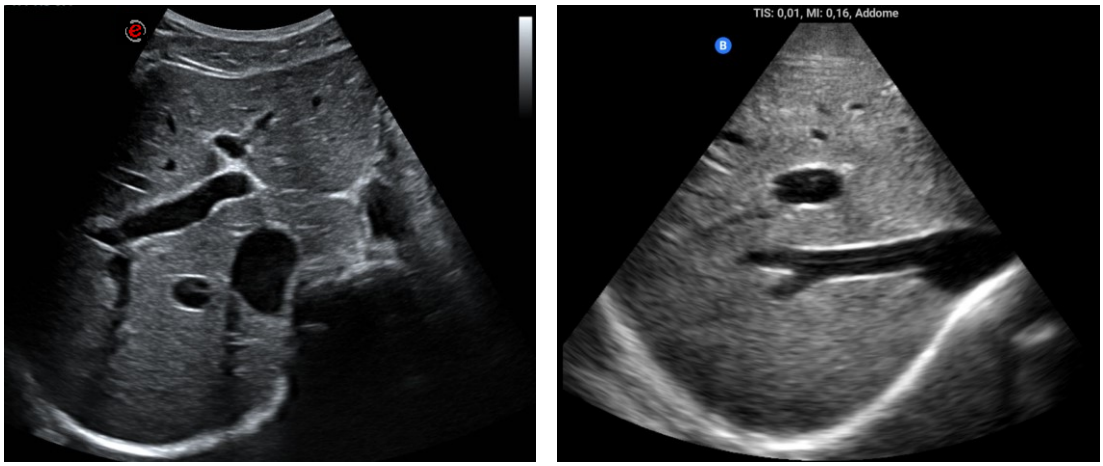

Figure 4.5. Liver ultrasound. Images from standard ultrasound machine (left) and from Butterfly iQ+ (right).

Example of liver ultrasound is shown in figure 4.5, representing the right lobe in oblique subcostal scan during different inhale phases. Despite images acquired by the two devices show two different liver planes, in both cases it is possible to evaluate liver and vessels structure. Liver is well defined, and its structure is very similar in both images. Over the anterior liver profile, it is possible to identify the fat layer and the underlying muscle; below the diaphragm profile is

recognisable. Portal vessels have perfectly defined hyperechoic walls, as well as the right suprahepatic vein in Butterfly iQ+ image.

4.3 Clinical evaluation results

This study has proved that images acquired with Butterfly iQ+ and standard ultrasound machine are qualitatively comparable, since they allow the identification of morphology, profiles, dimensions, and tissues of organs under examination, and also their interfacing with nearby vessels and organs. Images acquired for the study are general representations but looking at live ultrasound images during examination a congruence between images is still more significant.

It must be considered that in clinical practice even the most advanced ultrasound systems are not fully exploited, because sometimes maintenance services are neglected, and certain machines are kept alive although they are affected by obsolescence and their high performances decrease. Moreover, this study emerged the possibility of rooms for improvements in the image setting management in Butterfly iQ+ device, adjusting its few but essentials controls. As a result, it can be concluded that even if, from a quantitative point of view, certain parameters related to image quality in Butterfly iQ+ images are not at the same level of those related to a standard ultrasound machine, through appropriately trained physicians and by improving image setting management, it is still possible to obtain from Butterfly iQ+ enough adequate performances for making immediate diagnosis and performing in the POCUS practice.

Chapter 5

Conclusions

The aim of this thesis was the study of a handheld ultrasound device, Butterfly iQ+ system, based on a new technology that uses MEMS-based capacitive transducers to generate and receive ultrasound waves instead of traditional piezoelectric crystals. This technology allows for a remarkable cost reduction and the possibility to exploit the same transducer to emulate the three most used ultrasound pattern waves in one single probe, resulting in a great versatility and in a whole-body imaging. Its intuitive user interface, the incorporation of Artificial Intelligence-assisted tools, and the cloud storage used to archive and share patient data for remote consultations, definitely represent further advantages in the use of iQ+ device.

A key aspect that has been evaluated in this thesis is the image quality: a series of tests performed on a phantom have been conducted to provide an objective and quantitative assessment of certain parameters - image uniformity, contrast, and spatial resolution among others – all related to image quality. For this aim, Butterfly iQ+ has been tested and its parameter values have been compared with image quality indicators of a traditional ultrasound machines. Measurements and calculations of image quality parameters from both devices have been compared with real expected values, and committed errors have been evaluated acceptable or not according to the suggested tolerance limits provided by international quality control programs. Moreover, a statistical analysis with paired t-test has been conducted between image quality parameter values of both ultrasound systems, to emerge through statistical significances all inconsistent values between the two devices.

Results of this numerical evaluation of image quality in Butterfly iQ+ have shown very good performances in terms of distance measurements, with measurement values that are very near to the real ones and also statistically congruent to those of ultrasound machine used for comparison;

nevertheless, other image quality parameters like image uniformity and lateral resolution have provided mediocre results, for exceeding the suggested tolerance limits or for the highly dispersive results, and the worst image quality parameter is the contrast response.

Image quality with Butterfly iQ+ has also been evaluated from a qualitative point of view, since it is possible to go beyond the limitations quantitatively assessed, and thinking at Butterfly iQ+ probe as perfectly suitable for POCUS applications. For this purpose, another comparison between images has been conducted, but this time images have been acquired on normal organs of healthy subjects. Butterfly iQ+ application in clinical has revealed the possibility to consider its clinical images comparable to those of a traditional ultrasound system from a qualitative point of view, making iQ+ device suitable for immediate first level diagnosis according to POCUS methodical.

In conclusions, appropriate physicians' competencies and proper implementation of Butterfly iQ+ device can overcome its aspects related to image quality and provide adequate diagnosis wherever the patient is, even in remote places that have limited access to healthcare resources.

The worldwide success of Butterfly iQ+ device due to its disruptive technology has inspired other companies to work on new ultrasound devices based on similar concepts, accelerating the future development of many innovations in the ultrasound imaging field.

Bibliography

[1]. Rothberg, J., Hinz, W., Rearick, T. *et al.* An integrated semiconductor device enabling non-optical genome sequencing. *Nature* 475, 348–352 (2011). https://doi.org/10.1038/nature10242

[2]. Butterfly IQ gets FDA clearance for chip-based, smartphone-connected ultrasound. MobiHealthNews. https://www.mobihealthnews.com/content/butterfly-iq-gets-fda-clearance-chip-based-smartphone-connected-ultrasound

[3]. Butterfly Network Receives CE Mark for Handheld Butterfly iQ Ultrasound System. https://www.butterflynetwork.com/it/press-releases/butterfly-ce-mark

[4]. https://www.butterflynetwork.com/it-it/

[5]. https://www.butterflynetwork.com/press

[6]. B. T. Khuri-Yakub, O. Oralkan and M. Kupnik, "Next-gen ultrasound," in *IEEE Spectrum*, vol. 46, no. 5, pp. 44-54, May 2009, doi: 10.1109/MSPEC.2009.4907385.

[7]. https://www.butterflynetwork.com/iq

[8]. B. T. Khuri-Yakub, O. Oralkan. Capacitive micromachined ultrasonic transducers for medical imaging and therapy. J Micromech Microeng. 2011 May;21(5):54004-54014. doi: 10.1088/0960-1317/21/5/054004. PMID: 21860542; PMCID: PMC3158704.

[9]. Strickland E. New “Ultrasound on a Chip” Tool Could Revolutionize Medical Imaging. IEEE Spectrum 2017. https://spectrum.ieee.org/new-ultrasound-on-a-chip-tool-could-revolutionize-medical-imaging

[10]. https://support.butterflynetwork.com/hc/en-us/articles/360019540192-User-Manual

[11]. A window into the human body for less than $2000 enabled by breakthrough Ultrasound-on-a-Chip technology. https://www.butterflynetwork.com/it/press-releases/first-ultrasound-on-a-chip-receives-broadest-fda-510-k-clearance

[12]. https://vscan.rocks/it

[13]. https://www.philips.it/healthcare/product/HC989605450382/Trasduttore-ad-array-curvo-Lumify-C5-2

[14]. https://www.eenewseurope.com/news/handheld-ultrasound-scanner-pairs-ios-android-devices

[15]. http://www.sonostarmed.com/product/BWultrasoundScanner/Portable-B-Scanner/2015/0611/199.html

[16]. Xing Yu, Yaoyao Cui, Yuankai Xuan, Tingyi Jiang, Ligang Cui. Application and Development of Handheld Ultrasound in the Field of Medicine and Healthcare. Advanced Ultrasound in Diagnosis and Therapy, 2018, 2(2): 155-160.

[17]. https://www.cirsinc.com/products/ultrasound/zerdine-hydrogel/general-purpose-ultrasound-phantom/

[18]. https://www.universalmedicalinc.com/mwdownloads/download/link/id/631

[19]. Goodsitt MM, Carson PL, Witt S, Hykes DL, Kofler JM Jr. Real-time B-mode ultrasound quality control test procedures. Report of AAPM Ultrasound Task Group No. 1. Med Phys. 1998 Aug;25(8):1385-406. doi: 10.1118/1.598404. PMID: 9725125.

[20]. Fabiszewska E, Pasicz K, Grabska I, Skrzyński W, Ślusarczyk-Kacprzyk W, Bulski W. Evaluation of Imaging Parameters of Ultrasound Scanners: Baseline for Future Testing. Pol J Radiol. 2017 Dec 15;82:773-782. doi: 10.12659/PJR.904135. PMID: 29657644; PMCID: PMC5894034.

[21]. Sanders RC, Ledwidge M (2007) Basic physics. In: Clinical Sonography: A Practical Guide. 4th edn. Lippincott Williams and Wilkins.

[22]. Midiri M., Novario R., Martinoli C., 2004, Controlli di qualità in ecografia, SIRM. Available from https://areasoci.sirm.org/documenti_sirm

[23]. A. Scorza, S. Conforto, G. Lupi and S. A. Sciuto, "A texture analysis approach for objective uniformity evaluation in diagnostic ultrasound imaging: A preliminary study," *2015 37th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)*, 2015, pp. 6317-6320, doi: 10.1109/EMBC.2015.7319837.

[24]. Rampado O, Isoardi P, Ropolo R. Quantitative assessment of computed radiography quality control parameters. Phys Med Biol. 2006 Mar 21;51(6):1577-93. doi: 10.1088/0031-9155/51/6/015. Epub 2006 Mar 1. PMID: 16510964.

[25]. Kodak (2001) Guidelines for acceptance testing and quality control. *Kodak DirectView CR* 800 *and CR* 900 *System Technical and Scientific Bulletin.*

[26]. A. Rodriguez-Molares *et al*., "The Generalized Contrast-to-Noise Ratio: A Formal Definition for Lesion Detectability," in *IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control*, vol. 67, no. 4, pp. 745-759, April 2020, doi: 10.1109/TUFFC.2019.2956855.