Diagnostic Ultrasound Safety Review for Point-of-Care Ultrasound Practitioners

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Abbreviations
ALARA, as-low-as-reasonably-achievable; CEM, cumulative effective minutes; FDA, Food and Drug Administration; I_SPPA, spatial-peak pulse-average intensity; I_SPTA, spatial-peak temporal-average intensity; MI, mechanical index; PCH, pulmonary capillary hemorrhage; POCUS, point-of-care ultrasound; TI, thermal index; TIB, thermal index for bone; TIC, thermal index for the cranium; TIS, thermal index for soft tissue; US, ultrasound

Potential ultrasound exposure safety issues are reviewed, with guidance for prudent use of point-of-care ultrasound (POCUS). Safety assurance begins with the training of POCUS practitioners in the generation and interpretation of diagnostically valid and clinically relevant images. Sonographers themselves should minimize patient exposure in accordance with the as-low-as-reasonably-achievable principle, particularly for the safety of the eye, lung, and fetus. This practice entails the reduction of output indices or the exposure duration, consistent with the acquisition of diagnostically definitive images. Informed adoption of POCUS worldwide promises a reduction of ionizing radiation risks, enhanced cost-effectiveness, and prompt diagnoses for optimal patient care.

Key Words—as low as reasonably achievable; diagnostic ultrasound safety; Food and Drug Administration regulation; mechanical index; output display standard; point-of-care ultrasound; safety of the eye, lung, and fetus; thermal index; ultrasound bioeffects

Diagnostic ultrasound (US) has provided nonionizing radiation imaging for patient care for more than 50 years. In the past, the typical hospital diagnostic US machines were large cumbersome carts needing expert sonographers for production of useful diagnostic images, similar to computed tomographic or magnetic resonance imaging procedures. However, advances in design of US machines have reduced the size, while technological advances have improved image quality. In a radical departure from past practices, diagnostic US can now be easily portable and even "handheld": carried to the patient and applied by physicians or other trained individuals for an immediate assessment and diagnosis with real-time discussion, leading to enhanced patient service. This advance compares to the introduction and adoption of the iconic physician's stethoscope in the 19th century for auscultation and provides physicians with versatile US imaging of virtually any part of the body.[1] This development has created a new medical topic of point-of-care ultrasound (POCUS).[2] The appearance of POCUS research publications in the medical literature (PubMed) is rapidly increasing (Figure 1) and testifies to its scientific validation and growing importance in medical practice.

The use of POCUS has revolutionized the ability of clinicians to diagnose patients' conditions at the bedside rapidly and accurately. There are virtually no specialties in the house of medicine

that do not use US, either for diagnostic purposes or procedural guidance, or both. Training programs in a variety of fields and specialties offer advanced training with this specific imaging modality, and increasingly, US is incorporated into medical school curricula. Ultrasound offers a radiation-free, portable, and cost-effective means of imaging almost every part of the body.

Point-of-Care Ultrasound Patient Examinations

The rapidly expanding use of portable US machines allows diagnostic US examinations to be performed by the physician at the bedside.[3–5] The total use is impossible to determine because POCUS examinations are performed in so many settings, often without billing records and often routinely on a daily basis to follow patient progress.[6–8]

Rather than the comprehensive US examination that typically is performed in the radiology, obstetrics and gynecology, or cardiology suite, POCUS provides a rapid answer to a specific clinical question. The versatility of US is extensive; see Table 1 for a list of clinical conditions that potentially can be ascertained with US. For example, appropriately trained emergency physicians can effectively use US to accurately diagnose the conditions of patients who present to

Figure 1. Plot of the number of citations returned in a PubMed search for "point-of-care ultrasound" for each the last 15 years (*up to November 2019). The rapid development of POCUS research literature testifies to its growing importance in medical practice.

the emergency department, including those with conditions related to early pregnancy,[9] possible pericardial effusion,[10] abdominal aortic aneurysm,[11] undifferentiated shortness of breath,[12] and vision loss with retinal detachment[13] and those patients who have been traumatically injured.[14] The ability to perform and interpret these US examinations allows clinicians to diagnose potentially life-threatening conditions in a timely manner. In addition to the use of US in advanced health care environments, POCUS can be particularly beneficial in resource-poor locations. This modality can substantially alter management in places where other types of imaging are not available.[15,16] As an increasing number of physicians graduate from medical schools with knowledge of how to incorporate US into their clinical practices, it is expected that the use of this technology will continue to grow in a wide variety of health care settings.

Similar to adult medicine, pediatrics exemplifies the broad scope of POCUS being used in several disciplines, such as critical care, emergency medicine, anesthesia, surgical subspecialties, as well as outpatient and inpatient pediatrics. Furthermore, its use is being expanded to new environments such as urgent care. As the first imaging examination for many patients, POCUS is invaluable, as it provides real-time data that can be integrated into medical decision making. In addition, it has become an integral part of numerous procedures, including central and peripheral vascular access, incision and drainage of soft tissue disorders, nerve blocks, lumbar punctures, and bladder catheterization, among others. Furthermore, POCUS can be used either once or in an ongoing manner to monitor patients because of the lack of any accumulating dose effect (in contrast to ionizing radiation).

Benefits of POCUS are appreciated and endorsed by various societies, including the World Federation for Ultrasound in Medicine and Biology,[17] the American College of Emergency Medicine,[18] the Society of Critical Care Medicine,[19,20] and the American Academy of Pediatrics,[21] among others. However, the consideration of possible risks related to US exposure often is brief and lacking in rationale for safety guidance. Medical US originated as a means for tissue modification, and numerous applications of US for therapeutic purposes have been developed and are in extensive use.[22] Diagnostic US examinations must be
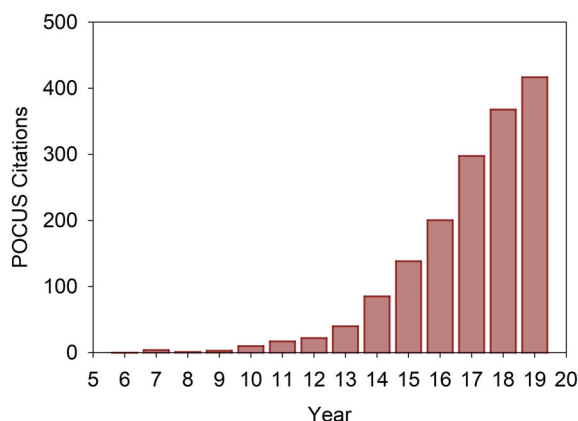
Table 1. List of Clinical Conditions That Can Be Potentially Ascertained With US at the Bedside

Head
    Skull fracture
    Neonatal interventricular hemorrhage
    Transcranial Doppler
Ocular
    Retinal detachment
    Vitreous hemorrhage
    Dilated optic nerve sheath (as manifestation of elevated
      intracranial pressure)
    Globe rupture
    Retrobulbar hemorrhage
Face
    Fluid in sinuses
    Peritonsillar abscess
Neck
    Lymphadenopathy vs abscess
    Thyroid masses
    Orotracheal airway evaluation
Cardiac
    Cardiac activity in setting of cardiac arrest
    Pericardial effusion
    Cardiac tamponade
    Estimation of left ventricular ejection fraction
    Focal wall motion abnormality
    Preload and response to therapy
    Evaluation of right ventricular function
Lung
    Pleural effusion
    Thoracentesis
    Interstitial alveolar syndrome
    Pulmonary edema
    Pneumothorax
    Acute heart failure
    Pneumonia
    Acute respiratory distress syndrome
Abdomen
    Biliary disease
    Hemoperitoneum
    Small-bowel obstruction
    Hernia
    Appendicitis
    Pyloric stenosis
    Intussusception
Pelvic
    Intrauterine pregnancy
    Ectopic pregnancy
    Ovarian masses
    Ovarian torsion
    Pelvic inflammatory disease
Genitourinary
    Hydronephrosis
    Testicular torsion
    Bladder volume (urinary retention)
Procedural
    Lumbar puncture

(Continues)

Table 1. Continued

    Central venous catheterization
    Peripheral vascular access
    Regional anesthesia
    Abscess localization
    Paracentesis
    Thoracentesis
    Procedural complications
Musculoskeletal
    Fractures: rib, extremity, skull
    Tendon injuries
Vascular
    Deep venous thrombosis
    Superficial thrombophlebitis
    Abdominal aortic aneurysm
    Aortic dissection
    Arterial thrombosis
    Inferior vena cava (volume assessment)
    Arterial access

configured carefully to avoid possible adverse consequences for the patient, through United States Food and Drug Administration (FDA) regulation and application of sonographer training.

The nonionizing radiation safety framework created by the FDA for ensuring the safe use of diagnostic US with guideline upper limits on acoustic output has proven its worth as a flexible and effective system.[23] There have been no established occurrences of patient injury by diagnostic US.[24,25] However, diagnostic US cannot be considered perfectly safe because of uncertainties about exposure dosimetry and potential injurious bioeffects. The safety issues are similar to those for all diagnostic US, but POCUS presents a new arena for ensuring the safe use of diagnostic US. The purpose of this article is to briefly review and discuss potential US exposure safety issues and to outline guidance for prudent use of POCUS. As this was a review of existing literature and did not require the use of animals or patient data, ethical approval and a request for obtaining informed consent were not required.

Background of Diagnostic US Safety Considerations

Thermal and nonthermal physical mechanisms are operative during US exposure.[26,27] There is essentially no risk of genetic injury from US (which exists for

ionizing radiation in radiography, positron emission tomography, and computed tomography). No universal dose quantity exists for US (such as the Gray, an ionizing radiation absorption quantity). The diagnostic US transducer emits pulses of US, which propagate into the body. There is no exposure to the operator or to bystanders because US does not transmit into or propagate well in air, and the exposure is only to the tissues interacting with the pulses. The risks of specific biological effects induced by physical mechanisms of tissue perturbation can be characterized by a threshold exposure response to the US output and duration, with zero risk below a threshold but an increasing impact above the threshold.[26]

Diagnostic US Exposure and Biological Effect Mechanisms

Figure 2 illustrates a US pulse and its acoustic parameters (measured in water). The waveform in Figure 2A displays the US pressure wave (for reference, atmospheric pressure is 0.1 MPa), which can be characterized by a peak rarefactional (negative) pressure amplitude and a mean frequency. The pulse carries momentum and has an intensity, calculated from the pulse waveform in units of watts per square centimeter (Figure 2B). Figure 2, C and D, illustrates the exposure at a focal point during B-mode imaging, as the scanning beam of US passes by the measurement point, for an interval of a few pulse repetition periods, and for 2 full image frames. Note that the US exposure is minimal most of the time at a given point (eg, the location of the small hydrophone used for pressure field measurement) for scanned beams, so that the overall temporal-average intensity is much lower than the pulse-average intensity. Directed fixed-beam modes (M-mode and pulsed Doppler mode) have much higher temporal-average intensities than imaging modes because the beam is not scanned. Ultrasonic energy is attenuated

Figure 2. Measured signals from a hydrophone in the scan plane of a 7.6-MHz diagnostic US transducer operated at an on-screen MI of 0.9 reduced (derated) to approximate the US values reaching a rat lung surface. The pulse waveform (**A**) is shown as pressure versus time, which is used to calculate the instantaneous and pulse-average (horizontal line) intensities (**B**). In **B**, the length of the line indicates a pulse duration of 320 nanoseconds. As the beam passes by the transducer, a series of pulses was received (**C**), which related to the scan rate and the width of the beam. The pulse repetition frequency in **C** was 10 kHz (100-microsecond repetition period). The imaging was continuous at 39 frames per second, which is seen as a brief series of pulses, as in **C**, repeated each 25.6 milliseconds (**D**) [Reproduced from Miller DL, 2016].
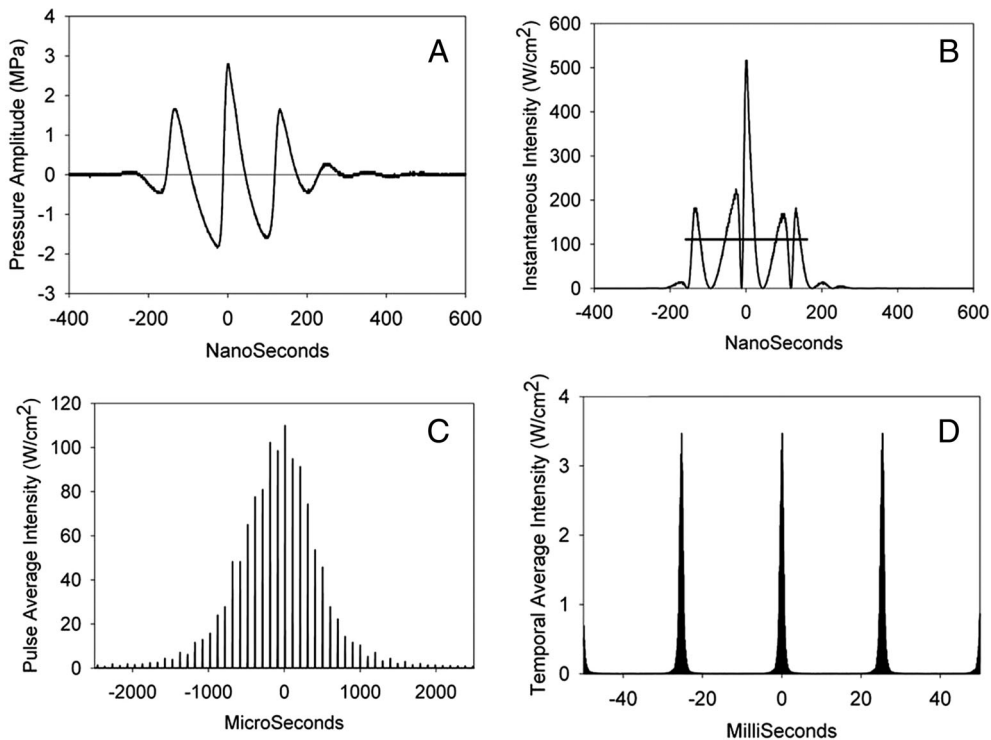
and absorbed in tissue depending on the absorption coefficient of the tissue. The attenuation is moderate for tissues such as liver, high for bone, and very high for lung and typically increases in proportion to the mean US frequency. Absorption of US in tissue results in an exponential decrease in the US intensity as a function of the propagation distance, which limits the penetration of US into the body and requires strong time-gain compensation to display images with depth uniformity. Even though the image appears uniform, the US exposure is much less for distal portions of an image relative to the focal point.

An assumption of safety for diagnostic US devices was codified by the Medical Device Amendments of 1976 enacted by the United States Congress. This act allowed for a simplified clearance process from the FDA of new devices that were substantially equivalent in safety and effectiveness to devices legally marketed for the same applications before May 28, 1976. This law led to development of protocols for measurement of diagnostic US outputs, for the setting of guideline upper limits on the output of diagnostic US devices, and eventually for the creation of exposure indices. Ultrasound machines are typically cleared for marketing by satisfying 510(k) premarket notification requirements of the FDA, including recommended upper limits to exposure parameters.[23]

The FDA identified the acoustic intensity of US as the key quantity for regulation and adopted the spatial-peak temporal-average intensity (I_{SPTA}) in milliwatts per square centimeter and the spatial-peak pulse-average intensity (I_{SPPA}) in watts per square centimeter for characterization. These quantities are calculated from measurements of the pulse pressure waveforms in water using a hydrophone (Figure 2). Furthermore, these measured values are used to estimate the peak intensities in scanned tissue by adjusting for tissue attenuation of the US, a process called derating. An attenuation coefficient of 0.3 dB cm^{-1} MHz^{-1} was adopted for this purpose as a conservative estimate of attenuation (typical tissues have higher coefficients) for safety. With the use of these methods and examination of pre-1976 devices, a table of maximal parameters was established for regulatory purposes. The values for the derated I_{SPTA} and I_{SPPA} ($I_{SPTA.3}$ and $I_{SPPA.3}$) are listed in Table 2 (mechanical index [MI] values are also listed; see "The Real-time Display of Acoustic Output" section below). Diagnostic US devices can be cleared

by the FDA by using these values via what is known as the track 1 method of obtaining marketing clearance. An important feature of this track 1 clearance method is that different recommended limits were established for different diagnostic US uses, with relatively low values for fetal (obstetric) and ophthalmic uses.

The Real-time Display of Acoustic Output

Track 1 was unsatisfactory in that devices approved by this method have no indication of the actual acoustic output and exposure (except that they should be less that the track 1 limits). In addition, the different values of $I_{SPTA.3}$ and $I_{SPPA.3}$ for different uses were not based on bioeffects studies because such information was not available. Rather, to assist in the FDA's decisions regarding substantial equivalence in terms of safety, they represented the maximum known output levels in each category for devices on the market before 1976.[28] Physicians can prescribe the use of an approved medical device for any examination deemed medically necessary, and the extent to which the track 1 limits have been followed in practice is uncertain. The US community, specifically the American Institute of Ultrasound in Medicine and the National Electrical Manufacturers Association, worked with the FDA to create a standard for displaying output indicators to the sonographer that had defined relationships with physical mechanisms for biological effects of US.[29] This output display standard was used to create a track 3 method for device approval (there is no track 2 method). This science-based method revolutionized the real-time assessment of exposure with direct

Table 2. Values of Recommended Maximal Output Exposure Levels for the 2 FDA 510k-Approved Tracks, Adapted From the FDA[23]

Use	$I_{SPTA.3}$, mW cm^{-2}	TI	$I_{SPPA.3}$, W cm^{-2}	MI
Preamendment acoustic output exposure levels (track 1)				
Peripheral	720		190	1.9
Cardiac	430		190	1.9
Fetal and Other[a]	94		190	1.9
Ophthalmic	17		28	0.23
Output display standard recommendations (track 3)				
Global Maximum	720		190	1.9
Ophthalmic	50	1.0		0.23

For both tracks, either the $I_{SPPA.3}$ or the MI limits may be used.
[a]Abdominal, intraoperative, pediatric, small organ (breast, thyroid, testes, etc), neonatal cephalic, and adult cephalic.

relevance to safety and mostly eliminated the arbitrary limits for uses of modern diagnostic US machines (Table 2), which can generally perform most of the different types of examinations.

The absorption of US energy in tissue leads to local tissue heating, thereby introducing a thermal mechanism with the potential for tissue injury. Thermal indices (TIs) were created to indicate the potential for heating during diagnostic US examinations. Heating is dependent on the tissue absorption coefficient, the temporal-average intensity, and the duration of the exposure at a particular point. As noted above, the relatively high I_{SPPA} is reduced by pulsing the US to the I_{SPTA}, and heating is further reduced by scanning the US beam and by the relative motion of the transducer and body. Heating is typically highest near the transducer and at the beam focus. The values of the TI capture the relative risk of thermal damage mechanisms during the US exposure.[30,31] Specifically, TI values translate the acoustic output of the US machine, quantified by the I_{SPTA}, into an estimate of the maximum potential temperature rise in degrees Celsius in the tissue for long dwell times (ie, the potential worst case). Since the US absorption properties vary based on tissue type, 3 different TI conditions have been defined. These are the thermal index for soft tissue (TIS) for soft tissue applications, the thermal index for bone (TIB) when bone is expected to be present in the imaging region of interest where the US waves are focused, and the thermal index for the cranium (TIC) when cranial bone is at the surface near the US transducer. As a gauge of the bioeffect risk, TI values of 0.7 or less can be considered inconsequential for any duration, whereas values of 6 or greater indicate a risk of tissue injury for 1 minute or longer durations and are discouraged by regulatory guidance.

There are also nonthermal mechanisms for effects of US on tissues. Acoustic radiation force, generated as US energy is absorbed, or acoustic radiation pressure, generated when US reflects from a surface, can cause perturbation of tissue.[32] The physical perturbations can be biologically substantial for high-intensity focused US[33] but are small for diagnostic US, with a minimal expectation of harm. Radiation forces can lead to fluid flow, which can be evident in a US image and useful for distinguishing cysts from tumors.[34] Radiation forces can also cause local tissue displacement within the focal beam and are the basis for elastographic

imaging. For the diagnostic US mode of shear wave elastography, radiation force impulses generate tissue displacement, which produces shear waves that are useful for mapping tissue elasticity.[35]

Acoustic cavitation describes the interaction of a US field with existing gas bodies or microbubbles and is another mechanism by which US can produce biological effects in tissue. Diagnostic US pressure amplitudes are sufficient (note that the peak negative pressure in Figure 2A of about 2 MPa equals a negative stress of 20 times the magnitude of atmospheric pressure) to warrant consideration of the possible occurrence of US inertial cavitation, which is associated with several biological effects. Inertial cavitation occurs when the US pulse interacts with a microscopic cavitation nucleus, such as a microbubble of gas. Above a peak rarefactional pressure amplitude threshold, the nucleus expands explosively to 2 or more times its initial diameter and then collapses under the inertia of the inrushing fluid. This phenomenon can kill nearby biological cells and damage blood vessels by mechanical processes and furthermore can cause damage by free radical generation due to temperatures exceeding 5000 K at the collapse point. By calculating the inertial cavitation thresholds for many different microbubble sizes and US frequencies,[36] minimum thresholds (for optimal nucleation) were found to increase as the square root of the frequency. This finding guided the creation of the on-screen MI, defined as the peak rarefactional pressure amplitude (derated for tissue attenuation) divided by the square root of the frequency and adjusted to in situ exposure. From the theory, the lowest threshold for inertial cavitation associated with the optimal size of nuclei (or microbubble) occurs at an MI of 0.4. However, the guideline upper limit of output for diagnostic US devices was set at an MI of 1.9. Of note, this limit value was determined from measurements of the output of a 2.25-MHz pre-1976 diagnostic US transducer and not by investigation of bioeffects and specific safety considerations.[28] The MI value of 1.9 thus tolerates a theoretical risk of cavitational bioeffects possible under optimal conditions of nucleation for MIs in the range of 0.4 to 1.9.

Current FDA 510(k) guidance for the output display standard (track 3) methods is given in Table 2. Manufacturers can choose to use either the $I_{SPPA.3}$ value or the MI value as the upper limit. (Note that

these limits are different, and, for example, the $I_{SPPA.3}$ can exceed 190 W cm^{-2} at an MI of 1.9 for US frequencies greater than about 2.25 MHz.). The 2 use categories are a global inclusion of most uses and ophthalmic use. The difference in the tracks is noteworthy for obstetric use: the I_{SPTA} limit was effectively increased from 94 to 720 mW cm^{-2}. The newer diagnostic US modes of elastography and contrast agent–enhanced diagnostic US were not noted specifically in the regulatory recommendations. However, elastography complies with the track 3 methods: the radiation force impulses are relatively long but have an MI of less than 1.9 and have an $I_{SPTA.3}$ of less than 720 mW cm^{-2} by virtue of relatively low pulse repetition frequencies (eg, ≤1 Hz). The modes used for contrast agent–enhanced diagnostic US fall under the recommendations in Table 2, and it is the microbubble-based agents that receive separate FDA approval as injectable drugs (with recommended US parameter limits noted in the package inserts). All US machines that display the safety indices have an explanatory document, *Medical Ultrasound Safety,*[37] included in the operator's instructions or other documentation as required by FDA regulations. The vendors of diagnostic US equipment should help supply safety information and to facilitate the prudent use of US exposure whenever possible.

As-Low-as-Reasonably-Achievable Principle

The dosimetry and thresholds for biological effects of diagnostic US are not definitively understood; therefore, uncertainty exists as to the possible risks of harm. Research on patient risks has been limited, and in fact, it is impossible to prove the absence of risk. Risk may depend on individual patient physiologic characteristics in addition to physical exposure parameters. To prudently accommodate these uncertainties, authoritative bodies assessing the diagnostic US safety problem have recommended the implementation of the as-low-as-reasonably-achievable (ALARA) principle.[26,38,39] The operator is responsible for implementing ALARA during US examinations. That is, the exposure duration and the acoustic output should be kept as low as reasonably achievable, consistent with collection of diagnostically acceptable images. The exposure indices were developed for display on diagnostic US machines to inform sonographers of exposure outputs related to thermal and mechanical (nonthermal) mechanisms,

described above. As a benchmark low-risk condition, diagnostic outputs (excluding ophthalmology) with an MI of less than 0.4[40,42] and a TI of less than 0.7[43,44] are considered to be of negligible risk of US-induced biological effects for any examination duration. Simple instructions for implementing ALARA are[38]: "Select the right transducer, start with a low output level, and obtain the best image possible by using focusing, receiver gain, and other imaging controls. If that is not adequate for diagnostic purposes, then increase the output level. We can further implement ALARA by reducing the total US exposure time." Diagnostic US may be used without reservation in most examinations for medical indications or for appropriate POCUS practitioner training.[45–47] However, ALARA should include the elimination of diagnostic US exposure with no medical purpose or benefit.

Safety Considerations for Specific POCUS Examinations

The possible risk varies greatly for different imaging modes, examination regions in the body, patient habitus, and health statuses. A reasonable application of ALARA to diagnostic US should include adjustment of exposure index values or the duration of the examination at hand by knowledgeable sonographers. The following considerations of various types of POCUS examinations help guide the safe use of diagnostic US.

Imaging Involving Low-Absorption Tissue Without Gaseous Nuclei

Many POCUS examinations are performed in adult tissues with low absorption, giving a TIS of less than 2, and no bodies of gas (Table 1).[48] The liver and kidney are commonly examined for abnormal masses and blood flow. The heart is examined by echocardiography for assessment of function. Small-parts imaging provides excellent images that can be presented at magnified image scales and typically do not include bone or bodies of gas. Focused assessment with sonography in trauma examinations can detect blood in the abdomen and pericardium (for lung, see the "Pulmonary POCUS" section below). Diagnostic interventional US for guided vascular access or fine-needle

aspiration is excellent for reduction of potential patient injury through control of the penetrating needle. Tissues in the body wall, including intercostal spaces and the abdominal wall, likewise have no bone or gas bodies in the imaging path.

Critically, the body does not appear to contain optimum cavitation nuclei for diagnostic US, likely because of the complete wetting and sterilization processes active in living tissue. Research on the occurrence of inertial cavitation in response to diagnostic US imaging of normal tissue has been negative, indicating that inertial cavitation–induced injury is nonexistent or very rare for diagnostic US without the presence of microbubble contrast agents. Therefore, the MI should be considered a general nonthermal exposure index, rather than a specific cavitation index (except for contrast-enhanced diagnostic US, discussed below).

These examinations also typically use imaging with low TI values (low temporal-average intensity) even at the maximum output. Heating is least for the low-absorption soft tissues (ie, other than bone or the cranium) and presents minimal risk of injury, particularly in adults, for a TI of less than 2, even for lengthy exposure times, as listed in Table 3. Therefore, the risk of injury from the thermal mechanism is also very low.

For low-absorption tissue without gaseous nuclei, the maximum output can be used with a very low risk of patient injury from the US exposure. The ALARA principle should still be applied when reduced-output imaging produces diagnostically optimal images to avoid higher exposures with no additional medical value.

Table 3. Recommended Limitations on Exposure Time for High-TI Settings of the Appropriate TIS, TIB, or TIC

TI Range, °C	Adult Scanning Time, min	Obstetric Scanning Time, min
>6	Not Recommended	Not recommended
5.0–6.0	<0.25	Not recommended
4.0–5.0	<1	Not recommended
3.0–4.0	<4	Not recommended
2.5–3.0	<15	<1
2.0–2.5	<60	<4
1.5–2.0	<120	<15
1.0–1.5	No time limit	<30
0.7–1.0	No time limit	<60
<0.7	No time limit	No time limit

Contrast-Enhanced POCUS

The use of US contrast agents to improve suboptimal US images and provide additional diagnostic information can be useful in several different situations, such as echocardiography and assessment of liver masses.[49,50] Contrast-enhanced diagnostic US requires venous access for contrast agent injection along with coordinated timing of the injection and imaging. Contrast agents are suspensions of stabilized microbubbles, which are designed for long circulation times and a strong echo response.

Contrast-enhanced diagnostic US has a known potential risk factor due to cavitation nucleation from the stabilized microbubbles.[51] This risk can be mitigated by the use of low-MI imaging modes (MI <0.4) designed for microbubble persistence and optimal contrast enhancement. However, there are also non–US-related risks, although rare, such as injection site complications, complement activation related pseudoallergy, and other anaphylactoid and allergic reactions.[40,50]

The use of contrast enhanced US is beginning to expand into the point-of-care setting, focusing on cardiac and trauma-related indications.[52,53] However, given the complex interaction of contrast agents, examination protocols, and system settings that can alter the cavitation risk, detailed safety parameters are beyond the setting of this review. In general, for imaging with contrast agents at an MI of greater than 0.4, practitioners should use the minimal agent dose, MI, and examination time consistent with efficacious acquisition of diagnostic information.

Head and Musculoskeletal Examinations With Bone and High-TI Modes

Musculoskeletal POCUS can be valuable for numerous diagnoses in head and musculoskeletal examinations (Table 1). A classic example of an important diagnosis perfectly suited to POCUS is an examination for rib fractures. Griffith et al[54] found that rib US was better at detecting rib fractures than chest radiography. Additional uses include assessment for skull fracture, neonatal interventricular hemorrhage, transcranial Doppler, fluid in the sinuses, etc.

These examinations are not expected to involve a cavitation risk. However, bone and tendon have high absorption coefficients and will heat faster and to higher temperatures than soft tissue. The TIB should be used for guidance when examinations involve bone,

and the TIC should be used for examinations of the head. For high-TI (>0.7) conditions, the exposure time should be limited during an examination. A multistep system is shown in Figure 3 and Table 3.[44,55] In febrile patients, the temperature elevation should be added to the on-screen TI to determine the exposure time. The exposure time limit decreases exponentially with an increasing TI (the horizontal scale in Figure 3 is logarithmic). Sonographers encountering higher TI values may advantageously reduce the TI (power output) to avoid hurried performance of difficult examinations. For a TI of 5, a 50% reduction in power (–3 dB, equivalent to an MI reduction, for example, from 1.4 to 1.0) cuts the TI in half, thereby allowing an exposure time of 1 hour rather than 1 minute.

Ophthalmic POCUS

Ocular US is used at the bedside to diagnose many ophthalmic conditions, including intraocular or periorbital foreign bodies, globe rupture, hyphema, lens dislocation, lens subluxation, retinal detachment, retinal hemorrhage, vitreous detachment, vitreous hemorrhage, choroidal detachment, papilledema, increased intracranial pressure, neoplasms, and vascular disorders.[56,57] The examination typically is conducted with a 7–15-MHz, small-footprint linear transducer coupled to the closed eyelid with a copious amount of gel to permit successful visualization without excessive pressure to the globe. If the US device lacks an "ophthalmic" preset, then frequently a "small-parts" preset is

Figure 3. Recommended TI versus exposure time safety guidance for the appropriate TIS, TIB, or TIC (Table 2). Note that on the logarithmic time scale, small changes in the TI result in large changes in the recommended time limit.
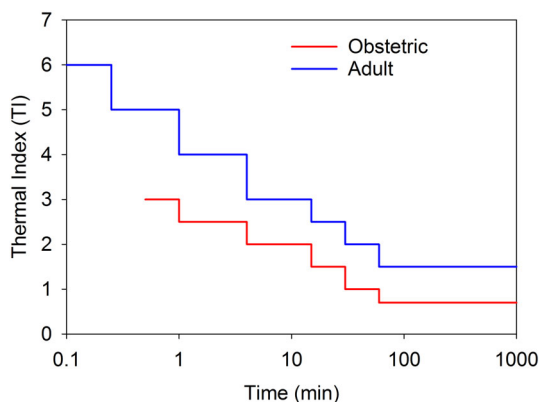
chosen. B-mode imaging is used for identifying anatomic abnormalities and the presence and location of foreign bodies, whereas Doppler US, both color and spectral, finds use in examining blood flow in the ophthalmic and central retinal arteries and veins.[56]

The possibility of both thermal and nonthermal bioeffects should be considered in the eye. In a review by van Rhoon et al,[58] safe thresholds for the temperature rise in various tissues and organs, including the eye, were expressed in terms of a thermal dose of cumulative effective minutes at 43°C (CEM43). The most sensitive eye structures were the lens, cornea, and retina, with the lowest CEM43 value being 2.4 minutes for the lens. One could base temperature-exposure time thresholds on this value or, alternatively, take a more conservative thermal dose-based approach by using the American Institute of Ultrasound in Medicine's "Statement on Mammalian Biological Effects of Ultrasound In Vivo"[42] for fetal exposures to set a CEM43 of 0.125 minutes for the eye. The eye and early first-trimester embryo have some comparable characteristics in that they can have a similar size; neither is well perfused; and protein is present.[59] However, a practical problem with either of these thermal dose approaches is that users only have access to the TI, not the actual temperature rise, and studies have found that the TIS could greatly underestimate the actual temperature rise in the eye.[60,61] The likely reason is that the generic tissue models used for the TIS are not appropriate for the eye, chiefly because of the relatively large absorption in the lens and orbital fat; also, the eye is poorly perfused. To offer some guidance, the British Medical Ultrasound Society has recommended not to exceed a TI of 1 when scanning the eye.[62]

Regarding nonthermal bioeffects, the eye normally has no gas body content. However, there are some clinical situations, such as trauma, surgery, or after the use of perfluorocarbon gases for treatment of retinal detachment, in which gas bodies might be present.[63] In these cases, the risk of cavitational nonthermal effects is possible.

Development of TI and MI recommendations for eye examinations is challenging because the aforementioned generic tissue models used for calculating these indices are not applicable to the eye. For this reason, the FDA diagnostic US guidance[23] has lower recommended maximum exposure levels for ophthalmic examinations of an $I_{SPTA.3}$ of 50 mW cm^{-2} or less, MI of 0.23 or less, and TI of 1 or less for devices that follow

the output display standard (Table 2). Temperature rise measurements in the eye due to US exposure have been described in several articles, which indicate that the risk of thermal injury is mitigated by the FDA guidelines for ophthalmic examinations.[61,63,64] Silverman et al[63] studied the safety of very high-frequency diagnostic US (US biomicroscopy) at 38 MHz and found no injury in histologic specimens for up to 30 minutes of exposure of a rabbit cornea or lens with an $I_{SPTA.3}$ of 34 mW cm^{-2} (ie, less than the FDA recommended limit of 50 mW cm^{-2}). In general, the eye should only be evaluated if there is an ophthalmologic preset on the system. If an ophthalmologic setting is not available, the patient should be informed that the scan is an off-label use and give appropriate informed consent.

Pulmonary POCUS

The first accepted use of pulmonary diagnostic US was to rule out pneumothorax.[65] Subsequently, diagnostic US has been found to be valuable in the diagnosis of pneumonia, pulmonary edema, pulmonary embolism, atelectasis, diffuse parenchymal disease, respiratory distress syndrome, and lung cancer.[66] The pleura appears in the image as a hyperechoic line. Artifacts are used to facilitate a variety of diagnoses, including B-lines (comet tail artifacts), which are diagnostic for pulmonary edema or interstitial lung disease.[67] Chest US is used in children for the diagnosis of neonatal respiratory distress syndrome,[68] pneumonia,[69–71] and other neonatal pulmonary diseases for which POCUS is used.[72] The assessments of B-lines and other image features are valuable in neonatal examinations for diagnosis of respiratory distress syndrome,[73] assessing surfactant treatment,[74] and pulmonary hemorrhage,[75] and the number of B-lines correlates with computed tomographic findings.[76] The total use of pulmonary diagnostic US is impossible to determine because POCUS examinations are performed in so many settings and often routinely on a daily basis to follow patient progress.

The biological effect of pulmonary capillary hemorrhage (PCH) produced by pulsed US exposure relevant to diagnostic imaging was discovered more than 25 years ago in mice[77] and has been confirmed in mice, rats, rabbits, pigs, and monkeys. Direct human bioeffect research ethically cannot be done, although an early clinical study (B-lines were not yet established as a lung US finding) was conducted to check for PCH on lungs of adult humans undergoing transesophageal echocardiography with exposure of the lung and thoracotomy, allowing lung examinations.[78] No hemorrhage was noted by the surgeon on gross examinations of the lungs. Recent results on the induction of PCH from diagnostic US imaging in rats were comparable to early results with laboratory pulsed US, and the US images displayed B-lines associated with the occurrence and progression of this bioeffect.[79,80] Animal research has shown that the PCH bioeffect depends on physical parameters, such as the US mode[81] and duration,[82] in addition to the MI. Biological factors also are very important, including sedation,[83] ventilation,[84] age and lung position,[85] and animal species.[86]

The physical mechanism for the PCH bioeffect is uncertain because both the thermal mechanism and cavitation have been ruled out, and a nonthermal mechanism such as acoustic radiation force or pressure may be important.[87] The most recent consensus report of the American Institute of Ultrasound in Medicine[88] states that, although it was clear that PCH might occur during realistic diagnostic exposures above an MI of 0.4, patient risk should be minimal for diagnostic US because only incidental lung exposure was expected. However, as noted above, pulmonary diagnostic US is now routine and widely performed using portable point-of-care machines. Clear application of the ALARA principle is needed.

Unfortunately, the B-line sign of PCH induction is not useful for safety guidance. The possibility of PCH induction for pulmonary examinations with an MI of greater than 0.4 likely can be excluded when no B-lines are seen, although very small PCH can escape detection.[82] However, the possibility of US PCH induction for pulmonary examinations with an MI of greater than 0.4 cannot be excluded when B-lines are seen because of ambiguity in the origin and persistence of the B-lines. B-line artifacts being sought for diagnostic indications and those being induced by the diagnostic US itself would be impossible to clearly distinguish, particularly in clinical examinations, because of the large variation in B-line appearances with lung sliding and hand motion of the transducer.

The prudent safety guidance for pulmonary US is to practice ALARA with an MI of less than 0.4 in many patients. Because the lung surface is often at a shallow depth, 0.7 cm even in some adults,[89] pulmonary images may be obtained at a reduced MI. An additional safety

margin exists for many pulmonary examinations, such as in high–body mass index patients, because the intercostal tissue has a relatively high absorption coefficient of about 1.2 dB cm^{-1} MHz^{-1} (which is higher than the value [0.3] assumed for the MI). The actual exposure at the pleura will be less than that indicated by the on-screen MI. For a chest wall thickness of 4 cm and a US frequency of 6 MHz, not an uncommon configuration, the exposure implied by the on-screen MI could be less by a factor of 10 at the visceral pleura, mitigating the risk of lung injury for an MI of greater than 0.4. These considerations should be factored into the patient-specific application of the ALARA principle, consistent with acquisition of diagnostically acceptable images.

Obstetric POCUS

Ultrasound is the imaging modality of choice for obstetrics and gynecology–related emergencies, as it can be used to rapidly identify the uterus and its contents. In addition, the adnexa can be evaluated, and the pelvis can be assessed for the presence of free fluid. Trans-abdominal US scanning will be the first approach, but transvaginal US will often be needed for its superior resolution. Common causes of acute lower abdominal pain in female patients include ovulation pain, ovarian torsion, hemorrhagic cysts, endometriosis, pelvic inflammatory disease, ectopic pregnancy, issues with an intrauterine contraceptive device, degenerating fibroids, as well as nongynecologic causes such as appendicitis. In obstetrics, POCUS can be used as a straightforward and accurate method to visualize an intrauterine pregnancy from 5 to 6 weeks' gestation to term. One of the most common indications for POCUS is abdominal pain in a patient with a positive pregnancy test result. In addition to location of the pregnancy, US can be used to confirm viability (presence of a fetal heartbeat), fetal number, and gestational age and, later in pregnancy, to assess the fetal presentation, growth, and well-being as well as the placental location, cervical length, and quantity of amniotic fluid.[90] Ultrasound is also used for prenatal imaging of fetal ocular and orbital abnormalities.[91]

Although there are no concerns with the use of US in gynecology, whenever there is the possibility of an intrauterine pregnancy, caution should be exercised.[59] The developing fetus is mostly susceptible to external insults in the first 10 to 12 weeks of pregnancy, the time of embryogenesis/organogenesis. The use of prenatal US for

inspection of the eyes also introduces the safety considerations for the eye, noted above in the "Ophthalmic POCUS" section. Importantly, a 20-year follow-up study of a randomized controlled trial found that no significant impact on visual outcomes or ocular biometry was associated with frequent in utero US (B-mode and spectral Doppler mode, likely including ocular exposure).[92] The occurrence of cavitational bioeffects or pulmonary capillary injury in the fetus is unlikely because of an absence of cavitation nuclei and the lack of gas in the fetal lungs and bowels. However, heat is a known teratologic agent, from animal research as well as from the described incidence of fetal anomalies in human mothers with an elevated temperature from infection early in pregnancy or secondary to an excessive use of hot baths or saunas. Therefore, precaution is necessary, particularly in modes that can generate higher acoustic outputs, such as the spectral (pulsed) Doppler mode. This has led to a joint statement recommending against the routine use of pulsed Doppler US in the first trimester.[39] In keeping with the ALARA principle, this would advocate for using the M-mode and not using the pulsed Doppler mode for measurement of the fetal heart rate alone.

The general recommendation should be to keep the examination as short as possible, with acoustic outputs as low as possible but sufficient to arrive at the correct diagnosis (ALARA principle). The TIS should be used before 10 weeks and the TIB after 10 weeks. Detailed advice on the maximum scanning time for a given TI is listed in Table 3. As for the adult case, a reduction in output can greatly lengthen the recommended scanning time limit. For example, a reduction in output power of 50% for a TI of approximately 3 reduces the TI to approximately 1.5, thereby allowing an exposure time of up to 30 minutes rather than less than 1 minute.

Discussion of US Safety in the POCUS Perspective

Reduction in the Ionizing Radiation Dose

This review has focused on safety considerations for nonionizing US exposure. However, it should be noted that POCUS has no risk of bioeffects such as cancer and no trend for increasing risk with exposure accumulation, as are well known for ionizing radiation doses. This feature of a US examination provides an overall

benefit by reducing the ionizing radiation dose. Point-of-care US is growing throughout all medical specialties, including pediatrics. Historically, US in pediatrics was used in traditional ways by both radiology and cardiology. The goal of bedside US, also known as POCUS, is to provide real-time information to clinicians at the point of care to guide medical decision making and provide procedural guidance. It is well established that radiation exposure in children has long-term effects.[93–97] The use of US can reduce the ionizing radiation exposure substantially. For example, POCUS has proven to be of value for monitoring Crohn disease in children[98] and can greatly reduce the cumulative ionizing radiation dose over the long course of this disease.[99]

Hands-on Training for High-Quality POCUS

The most important factor for POCUS efficacy and safety is operator training. Physicians and other medical personnel who may use POCUS must understand the principles of US imaging, the use of the exposure indices, and how to produce images of diagnostic value. Missed or incorrect diagnoses can have substantial adverse consequences for the patient. Numerous training guides are available, for example, in surgery residency,[100] anesthesiology,[101] pediatrics,[102] emergency medicine,[18] resource-limited emergency physicians,[103] critical care,[19] and clinical practice.[104] Hands-on training is critical and represents an important medical application of diagnostic US (with attention to potential incidental findings of medical importance).[46,47] Ultrasound imaging has become more and more clear and accurate but will show nothing of value in the wrong hands. A particularly exciting aspect of POCUS is that appropriate training including safety and image interpretation potentially can be given to many nonphysician medical personnel and can bring the benefits of POCUS to virtually any patient in need: for example, in remote rural areas.[105,106]

Summary of POCUS Safety Guidance

Diagnostic US exposure is regulated for safety, and US may be used without reservation in most examinations for medical indications or for appropriate POCUS practitioner training. Nonmedical uses should be minimized or avoided.[45] No diagnostic US–induced adverse biological effects have been demonstrated or confirmed in humans, but very little definitive human experimentation has been performed (because of problematic ethics and low sensitivity). Based on theoretical considerations and definitive animal studies, special attention and prudent use of the ALARA principle should be considered in 3 situations. The eye is particularly vulnerable and has special, separate FDA guidelines (Table 2), which must be set by the user for most US machines. The surface of the lung is excellent for a diagnostic examination but may have a risk of capillary hemorrhage in some patients who are thin or treated by some medications. The fetus, as always, must prudently be considered to be vulnerable and examined with care by using the correct TI value for exposure limitation. Sonographers themselves must practice ALARA patient exposure during POCUS examinations. Remembering these special situations may be aided by the acronym SAFE (safety of the eye, lung, and fetus).

Point-of-care US represents a revolution in patient care with timely and high-value diagnostic information. It is cost-effective and can fill the need for medical imaging in many venues, including the most remote settings. With few areas of concern for US exposure, the use of POCUS can reduce patient exposure to ionizing radiation, which is an overall benefit for patient safety. Continued growth and acceptance of POCUS will provide optimum patient care.

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