INTERNATIONAL GUIDELINES AND REGULATIONS FOR THE SAFE USE OF DIAGNOSTIC ULTRASOUND IN MEDICINE

Ng Kwan Hoong, PhD, DABMP
Department of Radiology
University of Malaya Medical Centre
Kuala Lumpur

Outline

- **Ultrasound Biophysics and Bioeffects**
- **Is there a risk?**
- **Development of Regulation and Safety Guidelines**
- **Benefits and Risks – the ALARA**
- **International Standards and Guidelines**
- **Conclusion**

Ultrasound Biophysics and Bioeffects

Ultrasound Biophysics and Bioeffects

- When ultrasound propagates through human tissue, there are potential biological effects or bioeffects.
- Very extensive research aimed at understanding basic mechanisms and evaluation of potential for tissue injury.
- Many studies are dose-effect studies and virtually all ultrasound-induced adverse bioeffects have occurred at higher intensities than diagnostic ultrasound.

Excellent review articles and books on the biological effects and safety of diagnostic ultrasound

1. AIUM, Bioeffects Considerations for the Safety of Diagnostic Ultrasound, Journal of Ultrasound in Medicine 7/9 Supplement, 1988.
2. AIUM, Bioeffects and Safety of Diagnostic Ultrasound. 1992.
3. AIUM, Bioeffects Committee: Bioeffects and Safety of Diagnostic Ultrasound, 1993.
4. AIUM, Mechanical Bioeffects from Diagnostic Ultrasound: AIUM Consensus Statements, Journal of Ultrasound in Medicine 19/2, 2000.
5. BARNETT SB (ed), WFUMB Symposium on Safety of Ultrasound in Medicine. Conclusions and Recommendations on Thermal and Mechanical Mechanisms for Biological Effects of Ultrasound. Ultrasound Med Biol, 24, Supplement 1, 1998.
6. BARNETT SB. Biophysical Aspects of Diagnostic Ultrasound. Ultrasound Med Biol. 26, Supplement 1, S68-S70, 2000.
7. BARNETT SB AND KOSSOFF G (eds), Safety of Diagnostic Ultrasound, Progress in Obstetric and Gynecological Sonography Series, 1998.
8. TER HAAR G AND DUCK FA, The Safe Use of Ultrasound in Medical Diagnosis, British Medical Ultrasound Society, British Institute of Radiology, 2000.

Mechanisms for ultrasound bioeffects

Thermal Non-thermal Others

Thermal Effects

As sound beam passes through tissue, it undergoes attenuation. A significant fraction of this attenuation is due to absorption. For low power ultrasound, the heat deposited is quickly dissipated.

Some concern is warranted with pulsed Doppler and color flow imaging equipment where high power levels and time average intensities may result in large values in thermal index.

Non-thermal (mechanical) Effects

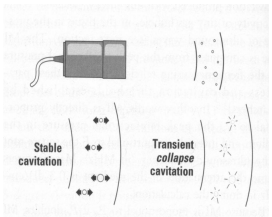
Cavitation : generation, growth, vibration and possible collapse of microbubbles within the tissue.

Two types of cavitation exist:

Stable cavitation - creation of bubbles that oscillate with sound beam;

Transient cavitation - process in which the oscillations grow so strong that the bubbles collapse violently, producing very intense, localized effects.

Cavitation mechanism



Cavitation is activity associated with tiny bubbles in the sound field.

- Stable
- Transient (collapse)

Zagzebski 'Essential of Ultrasound Physics'

Is there a risk?

Three sources of information on ultrasound bioeffects

- Epidemiology
- *in vitro* cell studies
- Animal studies

Epidemiology

- No adverse effects, including no evidence of low birth weights from diagnostic ultrasound have been demonstrated.
- AIUM [92] evaluated epidemiological studies and concluded:

  Widespread clinical use over 25 years has not established any adverse effect arising from exposure to diagnostic ultrasound.

  Randomized clinical studies are the most rigorous method for assessing potential adverse effects of diagnostic ultrasound.

Epidemiology

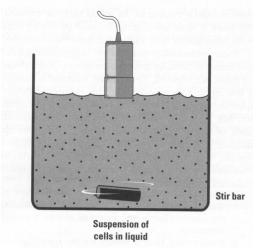
- Studies using this methodology show no evidence of an effect on birthweight in humans. Other epidemiology studies have shown no causal association of diagnostic ultrasound with any of the adverse fetal outcomes studies.

in vitro cell studies

- *in vitro* studies generally expose macromolecules, membrane transport systems, cells, or clumps of cells suspended in liquid.
- AIUM [92] : Although the exposure conditions and mechanisms are different from *in vivo* situations, an *in vitro* effect must be regarded as a real effect of ultrasound. *In vitro* studies also provide the capability to control experimental variables.

  One should be cautious with reports of *in vitro* studies that claim direct clinical significance.

in vitro cell studies



Exposure arrangement for in vitro experiment on cells

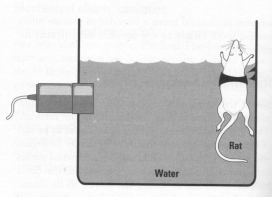
Zagzebski 'Essential of Ultrasound Physics'

Animal studies

- Most of the studies were done at I_{SPTA} and exposure times that exceed diagnostic values. At high time average intensity levels fetal weight reductions in rats, death of rat fetuses, and altered mitotic rates were observed. For these effects to be produced, animals are exposed to some minimal time average intensity for a given time.

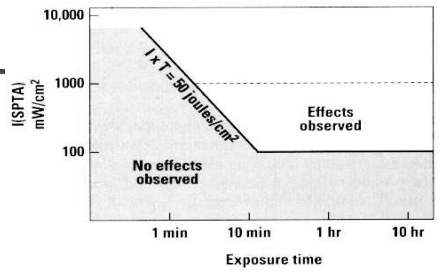
  If the intensity is reduced, the exposure time had to be increased to compensate for the reduced acoustic energy.

Animal studies



Typical exposure arrangement to study effects of ultrasound on animals and animal models

Zagzebski 'Essential of Ultrasound Physics'



Production of bioeffects in mammalian tissue. AIUM has claimed that no bioeffects were observed for intensities as high as 1Wcm^{-2} for ~~highly focused~~ beams (dotted line).

Development of Regulation and Safety Guidelines

- Unlike ionizing radiation, there has been little international safety standard on the clinical use of ultrasound or standard for the calibration of output from diagnostic equipment.
- FDA introduced application-specific limits on acoustic output for USA only.

  The permissible limit was lowest for ophthalmic (17 mW/cm^2, I_{SPTA}) and fetal (94 mW/cm^2 (I_{SPTA}) exposures where the tissues are particularly sensitive to damage.

- There is a large body of scientific literature on bioeffects but it is difficult to interpret much of the early work in the context of the safety of diagnostic ultrasound as the exposure conditions used were not clinically relevant.
- Difficult to find biological endpoints that were sufficiently sensitive to respond since modest acoustic outputs were used.

The Bioeffects Committee of AIUM [92]

- There is no evidence of independently confirmed adverse significant biological effects in mammalian tissue exposed *in vivo* to intensities (I_{SPTA}) below 100 mW/cm^2.
- Situation became more complicated when it was first reported [98] that bleeding could be induced in lung capillaries in animal following exposure to diagnostic levels of ultrasound at average intensities far below 100 mW/cm^2. This finding has subsequently been verified in other animal species.

Maximum Allowable Output FDA (USA)

Application-specific	ODS Track 3		
	I_{SPTA} (mW/cm^2)		MI
Peripheral vessel	720	720	1.9
Cardiac	430	720	1.9
Fetal, neonatal	94	720	1.9
Ophthalmic	17	50	0.23

AIUM/ NEMA Output Display Standard (ODS) - 1992

- For each ultrasound examination a Real Time On Screen Display indicates 'risk' of producing bioeffects:
- TI = Thermal Index (relates to avg. intensity)
- MI = Mechanical Index (relates to cavitation – peak pressure)

What is TI?

TI is the ratio of acoustical power produced by the transducer to the power required to raise the temperature in tissue 1 ^{o}C.

A TI value of 1 means that under tissue conditions assumed in the algorithm, a 1^{o} elevation of temperature is possible.

FDA : TI < 6

What is MI?

MI value is computed from the peak rarefactional pressure and the frequency, and is intended to estimate the potential for mechanical bioeffetcs.

The higher the index value, the higher is the probability of a bioeffect occurring. Values less than '1' is generally considered to be 'safe'.

FDA : MI < 1.9

- TI estimates the potential for producing thermally-induced bioeffects in soft tissue and bones

TIS	soft tissue	cardiac,1st trimester fetal
TIB	bone near focus	2nd & 3rd trimester fetal
TIC	bone near surface	transcranial

- MI estimates the potential for producing non-thermal/mechanical bioeffects in tissue.

Limitations of ODS (FDA)

- Underestimate MI in non-linear mode
- Underestimate TI in some fetal exposures
- TI is displayed for Doppler, but not included for duplex/ multimode
- TI has no duration factor

Limitations of ODS (FDA)

Due to the difficulties of estimating tissue conditions, these indices provide indicators of risks rather than quantifiable values. They do not take into account factors such as dwell time, examination time, patient temperature or presence of contrast agents.

Benefits and Risks - the ALARA

Benefits vs. Risks

- No question on benefits from diagnostic ultrasound. However we must bear in mind the the potential risks.
- Other risk to be considered:

  the risk of not doing the ultrasound examination and either not having the information, wrong information, or having to obtain it in a less desirable or invasive way.

  Attention must now be focused to evaluate the cost of morbidity arising from the use of sub-optimally performing equipment in diagnosis and management.

How do we balance Benefits and Risks?

Prudent use can be achieved by applying the simple concept of ***ALARA,***

i.e. As Low As Reasonably Achievable

Following ALARA principles

⇒ we keep total ultrasound exposure as low as reasonably achievable, while optimizing diagnostic information.

Controls the operators can adjust to improve image quality and minimize output intensity

- Controls that directly affect intensity are application selection and output intensity.
- The controls that change the characteristics of transmitted ultrasound field and indirectly affect intensity are system mode, pulse repetition frequency, focusing depth, pulse length and transducer choice.
- The 'receiver controls' help to improve image quality only are receiver gain, TGC, video dynamic range and post processing.
- Philosophical aspect of ALARA - minimizing scan time, performing only required scan, and never compromising quality by rushing through an examination.

Advice to operators

- Because the threshold of bioeffect intensity is not known, it is the responsibility of the operators to use his/her judgment and insight to adjust the intensity output of the equipment so as to get the most information at the lowest output power.

AIUM's complete statement on Clinical Safety Bioeffects Committee: Bioeffects and Safety of Diagnostic Ultrasound [93]

"Diagnostic ultrasound has been in use since the late 1950's. Given its known benefits and recognized efficacy for medical diagnosis, including use during human pregnancy, the AIUM herein addresses the clinical safety of such use:

No confirmed biological effects on patients or instrument operators caused by exposure at intensities typical of present diagnostic ultrasound instruments have ever been reported. Although the possibility exists that such biological effects may be identified in the future, current data indicate that the benefits to patients of the prudent use of diagnostic ultrasound outweigh the risks, if any, that may be present."

International Standards and Guidelines

WORLD FEDERATION FOR ULTRASOUND IN MEDICINE AND BIOLOGY

U.S. Department of Health and Human Services Food and Drug Administration

AMERICAN INSTITUTE OF ULTRASOUND IN MEDICINE

ASUM Policies and Statements

European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB)

Statement on the safe use, and potential hazards, of diagnostic ultrasound.
Prepared by the Safety Group of the British Medical Ultrasound Society.

TER HAAR G AND DUCK FA, The Safe Use of Ultrasound in Medical Diagnosis, British Medical Ultrasound Society, London, British Institute of Radiology, 2000.

Some key aspects of guidelines and regulations

- World Federation for Ultrasound in Medicine and Biology (WFUMB)
- American Institute of Ultrasound in Medicine (AIUM)
- Australasian Society for Ultrasound in Medicine (ASUM)
- European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB)
- U.S. Food and Drug Administration (FDA)

World Federation for Ultrasound in Medicine and Biology (WFUMB) Guidelines

- B-mode Not contraindicated on thermal grounds when no gas present
- Doppler Use lowest available power consistent with obtaining good diagnostic information. Minimize time beam passes thro one point
- Thermal effects Temp rise ≤ 1.5° (38°C) can be used without reservation. Obstetric exposures resulting in a temp. increase of 4°C for 5min are potentially hazardous
- Non-thermal effects When gas (inc. contrast agents) is present exposure levels and duration should be reduced to the min. to obtain required information

International guidelines and recommendations are needed to address these areas of concern:

- Use of Doppler ultrasound in the first trimester
- Epidemiology especially obstetric examinations
- Non-clinical use of ultrasound imaging
- New application and technique such as harmonic imaging using contrast agents

Self-regulation

Self-regulation - move away from the FDA-enforced, application-specific limits on acoustic output to a system where bioeffects are assessed from the real-time display of safety indices.

This shift of responsibility of risk assessment from regulatory authority to the users creates an urgent need for continuing education and the awareness of safety issues.

The international ultrasound community must be ready for this change.

Conclusion

Safety Issues

- No convincing evidence that diagnostic ultrasound causes adverse health effects in human
- Epidemiology data has several limitations
- No data for modern powerful diagnostic equipment
  - operating with ODS
  - pulsed Doppler, harmonic imaging, contrast agent

Safety Issues

- New trend – operators responsible for benefit/risk analysis
- ODS has limitations – use as a guide only
- Bioeffects at diagnostic level – ΔT higher at bone
- Cavitation at tissue/gas interfaces or with contrast agents

Awareness and Education

It is important to create awareness of risk and the development of safety culture among practitioners.

There is a strong need for continuing education to ensure that appropriate risk/benefit assessments are made by practitioners based on current knowledge and pave the way for self-regulation.

AFSUMB to take action *NOW*

- AFSUMB should formulate guidelines for safe use of ultrasound and to endorse the guidelines and recommendations of WFUMB
- AFSUMB should participate actively in research on various aspects of bioeffects and safety.

AIUM 99 ‘Non-medical use’

“The AIUM strongly discourages the non-medical use of ultrasound for psychosocial or entertainment purposes. The use of ultrasound (2D or 3D) to only view the fetus, obtain a picture of the fetus or determine the fetal gender without a medical indication is inappropriate and contrary to responsible medical practice….”

Commercial Demonstration using pregnant ladies as models

- High intensity and long exposure
- We DON’T know the potential bioeffects on fetus
- Prudent medical use?