Ultrasound Mediated Bioluminescence Tomography for High Sensitivity, High Spatial Resolution 3D Imaging

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NC3Rs National Centre for the Replacement Refinement & Reduction of Animals in Research

1. Introduction

- Light offers an alternative to techniques such as X-rays, CT, PET or MRI for imaging body tissues.
- The main drawback of using light is its heavy scattering by tissue which makes image spatial resolution poor.
- Bioluminescence optical imaging (BLI) with ultrasound (US) can offer a significant improvement in spatial resolution over conventional BLI.
- The improvements in spatial resolution can be achieved in two ways:

1. **By modulating the bioluminescence light emitted within the tissue using focused US beam.**
2. **By using information provided by US imaging as a priori information in a DOT/NIRS reconstruction algorithm.**

2. Experimental Setup and Materials

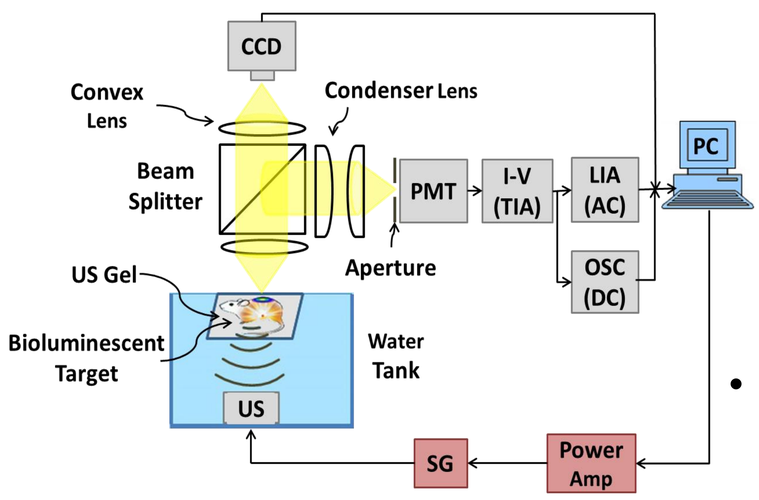

Fig.1 A Novel Small Animal US Mediated BLI Platform

- The photomultiplier tube (PMT) detects the US modulated BLI signals.
- CCD camera records the optical image for standard BLI.
- US scanning also allows to get 3D structural data.

Measurement of Modulated Incoherent Low Light Levels

- **Incoherent Light:** LED source (Thorlabs, LED635L, λ=635 nm), Chemiluminescent materials.
- **US transducer:** US V394 NDT, 1MHz, 75mm focal length).
- **Detection System:** PMT (Hamamatsu, H5783-20) based detection system.

3. Results

Characterization of US Modulated Bioluminescence Detection System

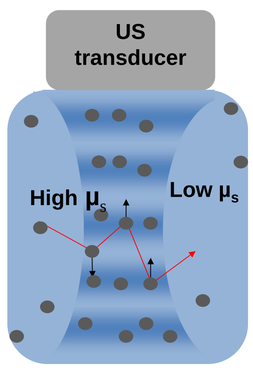

Fig.3.1 Mechanism of US modulation of scattered light

- **US induces variations in optical properties due to compression and rarefaction of the medium (tissue).**

$$\Delta n = n_0 \eta k US(t)$$

$$\Delta \mu_s' = \mu_{s0}'[1 + 0.37\eta] k US(t)$$

$$\Delta \mu_a = \mu_{a0} k US(t)$$

where Δn, $\Delta \mu_s'$ and $\Delta \mu_a$ are changes in the refractive index, reduced scattering coefficient and absorption coefficient respectively.

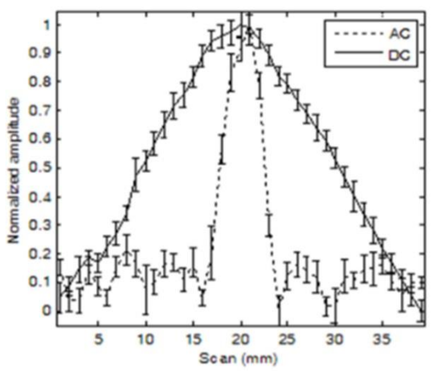

Fig. 3.2 AC (US modulated light) and DC (unmodulated light) line-scans of luminescent target embedded inside a tissue 'phantom' (Huynh NT *et al* J Biomed Opt, 2012).

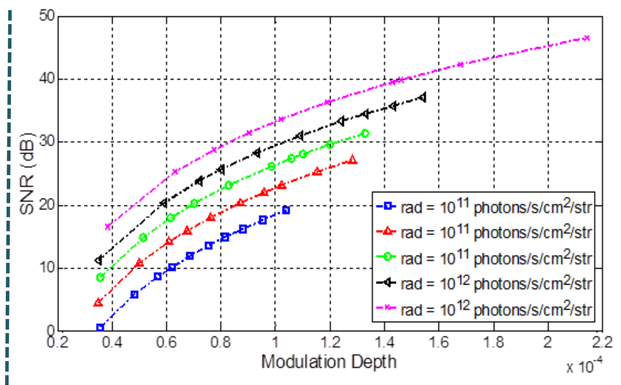

Fig. 3.3 Plot of Modulation depth vs SNR for a tissue 'phantom' having the product of scattering coefficient and thickness nearly equal 150 as that of a nude mouse.

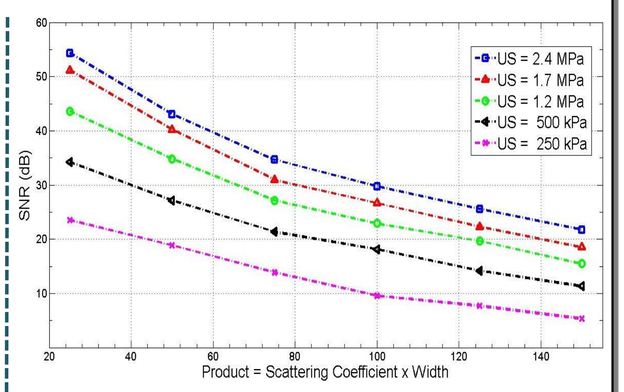

Fig. 3.4 At varying US pressures, SNR decreases with the increase in the scattering coefficient of tissue 'phantom'.

4. Discussion & Conclusions

- Small animal experiments are mimicked using tissue like 'phantom' of known optical and acoustic properties.
- Low level incoherent light sources having similar characteristics as a bioluminescent source with surface radiances ranging 10^6, 10^7 ,…,10^{11} (photons/s/cm^2/str) are embedded inside the tissue phantom.
- The systems is optimized with respect to spatial resolution and signal to noise ratio (SNR). High Spatial resolution can be achieved using pulse gating US and high frequency (HF), but this inevitably reduces the SNR due to small US focal volume.
- In a scattering medium, optimizing SNR is a difficult challenge with small US focal volume.

5. Future Work

- A set of in-vivo experiments on a nude mouse using bioluminescent probes.
- Employing contrast agents (liposomes etc.) with HF pulsed US to enhance SNR.
- Develop a software tool for the processing and 3D reconstruction of prerequisite data to be used as an input for proposed optical imaging.

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