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Photoacoustic Scanning Tomography (PHAST) with Coded Optical Excitation: Theory and Experiment

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Photoacoustic Tomography: Objectives and Methods

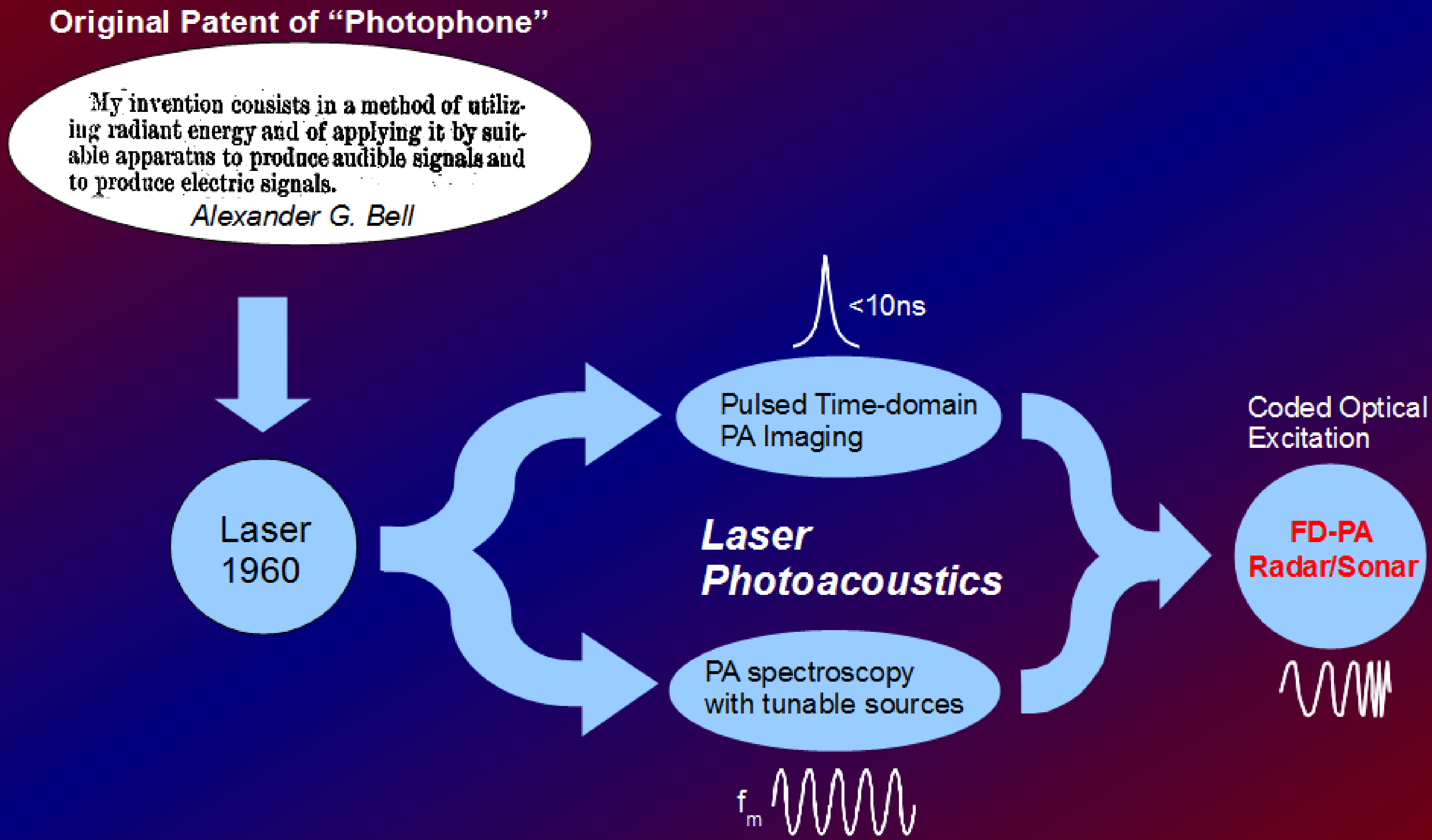
Imaging Objectives:

1. Positions and dimensions of photoacoustic (PA) sources.
2. Characteristics of PA sources: absorption coefficient, chemical composition, blood flow rate etc.

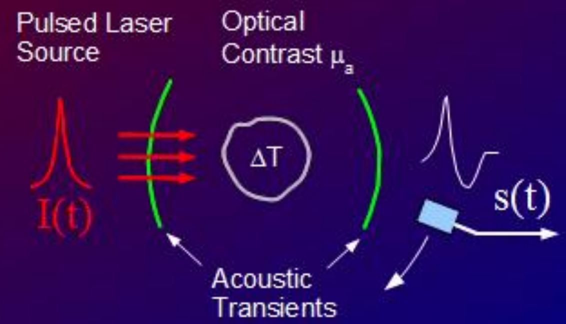
Standard PA Methods:

1. Short (nanosecond) laser irradiation and broadband detection.
2. Photoacoustic microscopy with high frequency (> 30 MHz) sources.
3. Photoacoustic spectroscopy with narrow band tunable sources.

Photoacoustics: Historical Developments



Pulsed Laser Photoacoustics



$$\nabla^2 p(\vec{r},t) - \frac{1}{c^2}\frac{\partial^2 p(\vec{r},t)}{\partial t^2} = \frac{-\beta}{C_p}\frac{\partial q(\vec{r},t)}{\partial t}$$

Confinement conditions:

$$\sqrt{D_T t_L} < \mu_a^{-1};\ t_L < \frac{1}{c\mu_a}$$

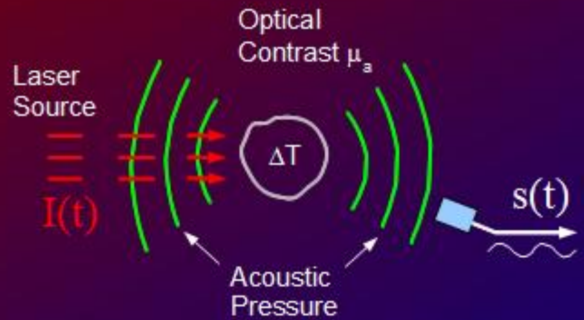
$$q(\vec{r},t) \approx \mu_a \Phi_0(\vec{r})\delta(t)$$

$$p_0(z) = \Gamma \mu_a \Phi_0 \exp(-\mu_a z)$$

Key Characteristics

- High magnitude acoustic transients
- Signal profile carries information on light absorption and chromophore dimensions
- Depth information obtained from “time-of-flight” measurements
- Relatively expensive laser source, especially with tunable wavelength and high repetition rate options
- Broadband ultrasound detection – excessive level of noise and interference

Photoacoustic Imaging with Intensity Modulated CW Laser Source (Frequency Domain PA)



$$\nabla^2 \tilde{p}(\vec{r},\omega)+k^2\tilde{p}(\vec{r},\omega)=\frac{-i\omega\beta}{C_p}\tilde{q}(\vec{r},\omega)$$

$$\tilde{q}(\vec{r},\omega)=\mu_a(\vec{r})I(\vec{r})\tilde{F}(\omega)$$

Confinement conditions in FD:

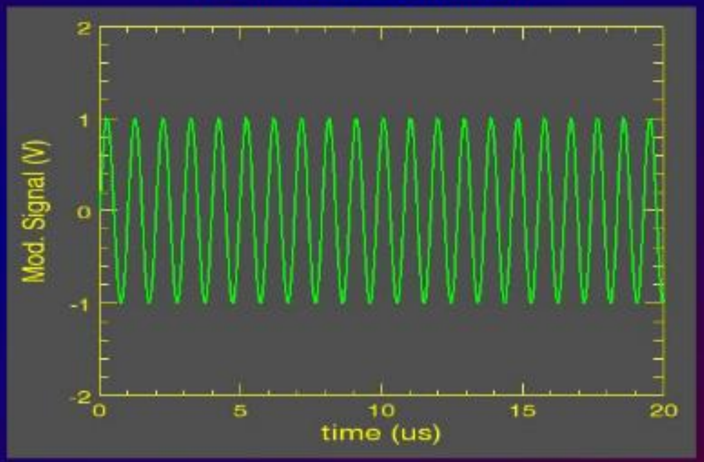
$$L_T=\left(\frac{D_T}{\omega}\right)^{1/2} \ll \mu_a^{-1}$$

$$\omega < \omega_a=\mu_a c_a$$

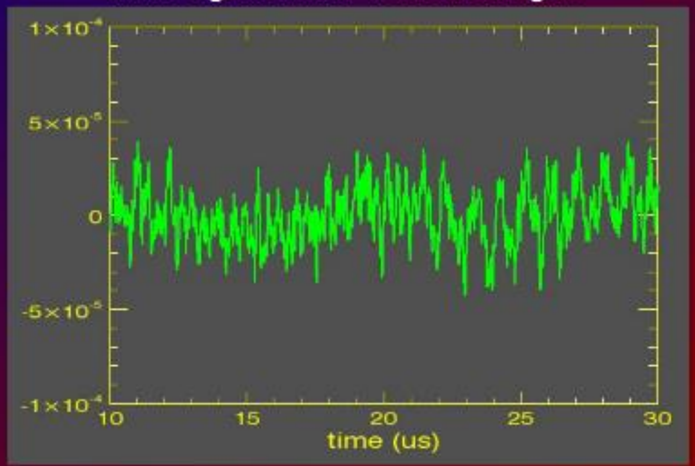
Difficulties of FD photoacoustics:

1. Low optical power (0.1 – 1 W) → Low SNR
2. Long pulse duration (> 1 ms) → Poor spatial resolution

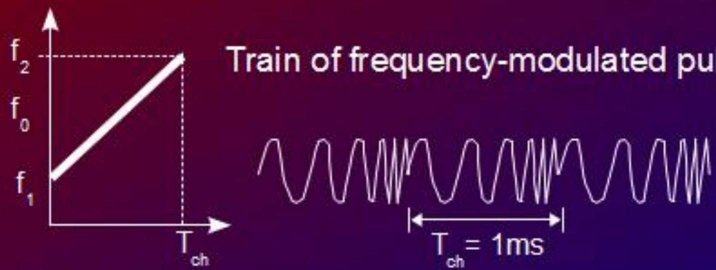
Modulation waveform



Raw signal after 1000 averages

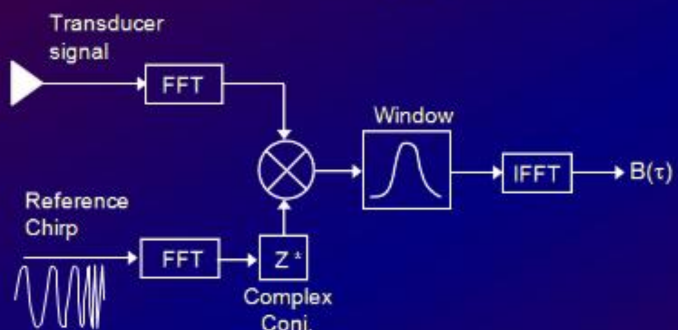


Spatially-Resolved PA Imaging with Chirped Waveforms – Photoacoustic Radar



Correlation Processor

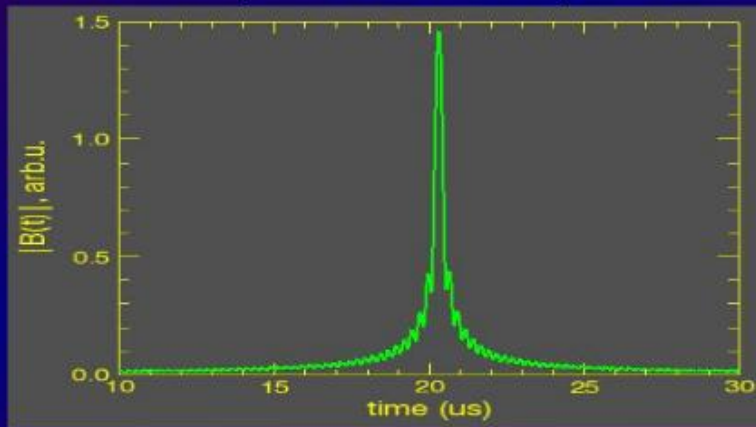
$$B(\tau)=\int_{-\infty}^{\infty} r(t+\tau)s(t)\,dt=\frac{1}{2\pi}\int_{-\infty}^{\infty}\tilde{R}^{*}(\omega)\tilde{S}(\omega)e^{i\omega\tau}\,d\omega$$



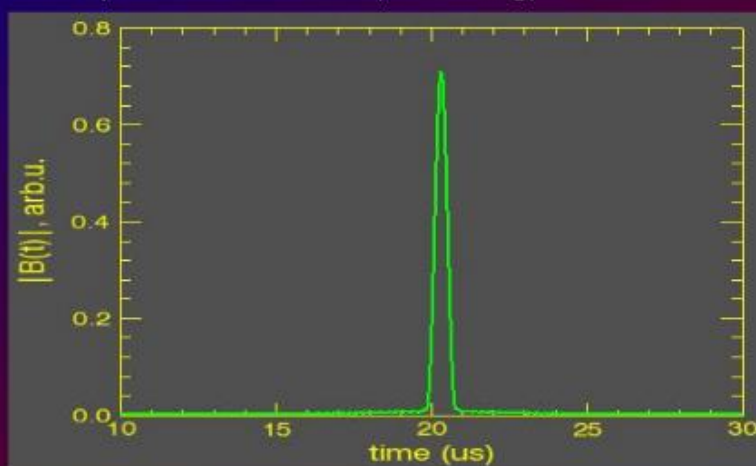
$$B(\tau)=\underbrace{\frac{A^{2}T_{ch}}{2}}_{\text{Peak Amplitude}}\;\underbrace{\frac{\sin\left[\frac{\pi m\tau}{T_{ch}}\left(1-\frac{\tau}{T_{ch}}\right)\right]}{\pi m\tau/T_{ch}}}_{\text{Side lobes}}\;\underbrace{\cos(\omega_0\tau)}_{\text{Harmonic carrier}}$$

$m = T_{ch}\Delta f$ - Time-Bandwidth product

Correlation amplitude of a linear chirp 1 – 5 MHz

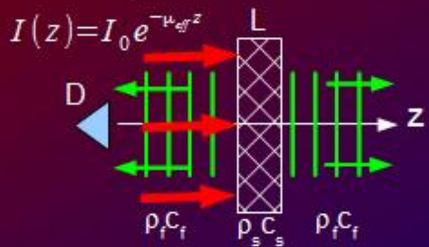


Spectral windowed (Hamming) correlation



Analytical Model of PA Generation

1-D Model with Acoustic Impedance Discontinuity



$$\tilde{p}_{zz}(z,\omega)+k^2\tilde{p}(z,\omega)=\frac{-i\omega\beta}{C_p}\tilde{q}(z,\omega)$$

$$\tilde{q}(z,\omega)=\mu_a I_0 e^{-\mu_a z}\tilde{F}(\omega),\quad \tilde{F}(\omega)$$ - Spectrum of the laser modulation waveform

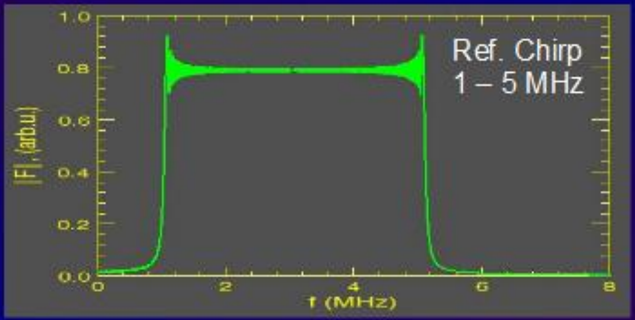
<u>Method of transfer functions:</u>

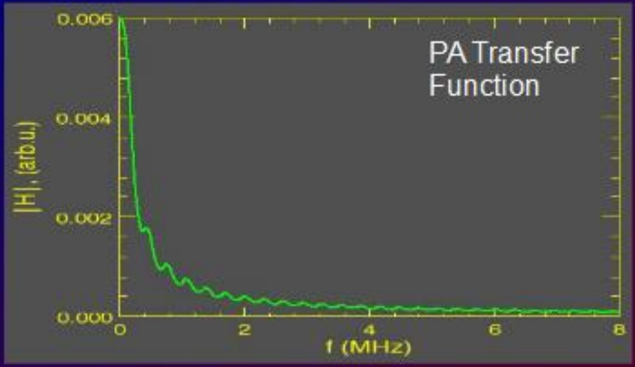
$$\tilde{p}(\vec{r},\omega)=\tilde{H}_{PA}(\omega)\cdot I_0\cdot\tilde{F}(\omega)\cdot\Phi(\vec{r})$$

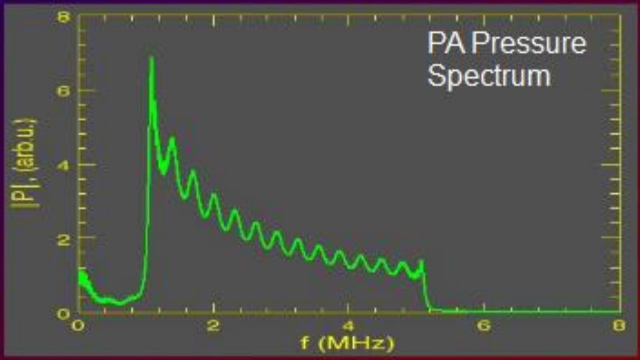
<u>1-D solution for exponential source:</u>

$$H_{PA}(\omega)=\frac{-i\beta\mu_a c_s}{C_p(\mu_a^2 c_s^2+\omega^2)}\cdot\frac{(\zeta k_f+i\mu_a)\cos(k_s L)+(i k_s-\zeta\mu_a c_s/c_f)\sin(k_s L)-(\zeta k_f+i\mu_a)e^{-\mu_a L}}{i(1/c_s^2+\zeta^2/c_f^2)\sin(k_s L)+(2\zeta/c_s c_f)\cos(k_s L)}$$

$$\tilde{p}(z,\omega)=\tilde{H}_{PA}(\omega)\cdot I_0\cdot\tilde{F}(\omega)\cdot e^{-ik_f z},\quad k_f=\omega/c_f$$







Correlation Processing of Chirped PA Signals

<u>*Simulation Results for a 1-D layer:*</u>

Layer thickness: 5 mm
$\rho_s c_s$ = 1.54 MRyals
$\rho_f c_f$ = 1.48 MRyals
Absorption: 4 cm^{-1}

Optical Modulation:
Sine chirp: 1 – 5 MHz
Chirp duration: 1 ms

Zero-mean Gaussian noise:
Input SNR = - 40 dB

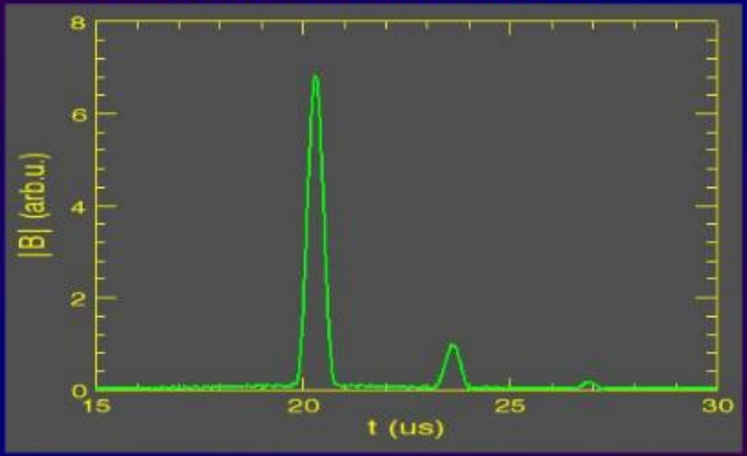
Coherent averaging of 1000 chirps

Axial Resolution: $c_a/\Delta f$ < 1 mm

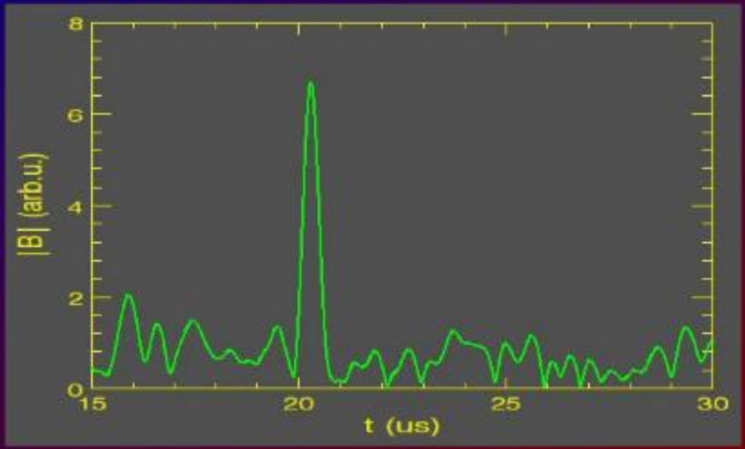
SNR Improvement ~ 56 dB

Estimated SNR of the pulsed PA under the same conditions exceeds that of CW by ~ 10 dB

Noise-free correlation function



Correlation function of noisy signal



Correlation Processing for a Distributed Source

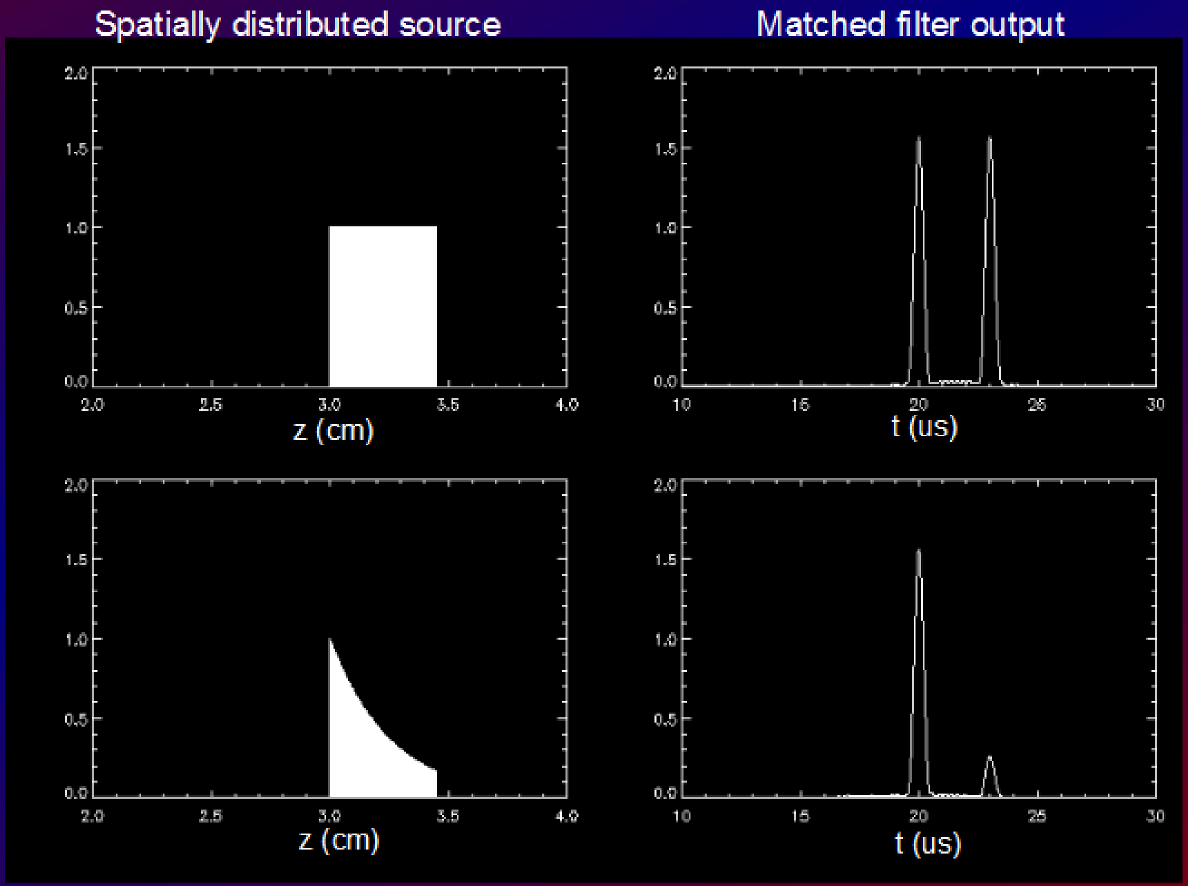
PA Source:

$$q(z,t) = \mu_a I_0 e^{-\mu_a (z - z_0)} f(t)$$

f(t) – linear chirp

1. Uniform distribution (weak absorption)

2. Exponential distribution $\mu_a = 4\ cm^{-1}$



Discontinuities of source function produce correlation peaks

Signal-to-Noise of Frequency Domain PA Measurements

Matched Filter (Correlation):

$$B(\tau)=\frac{1}{2\pi}\int \tilde{R}(\omega)\tilde{S}(\omega)e^{i\omega\tau}d\omega$$

$$|B(\tau)|=\sqrt{\Re^2 B(\tau)+\Im^2 B(\tau)}$$

Gaussian noise PSD:

$$N_0=\frac{\langle P_N\rangle}{f_s/2}=\frac{2\sigma^2}{f_s}$$

Noise of matched filter (Rayleigh distribution):

$$PDF=\frac{A}{\sigma_A^2}\exp(-A^2/2\sigma_A^2)$$

$$E[A]=\sqrt{\frac{\pi}{2}}\sigma_A,\sigma_A{}^2=\frac{E_s\sigma^2}{f_s}$$

$$Var=0.43\sigma_A{}^2$$

SNR of Matched Filter (Single Chirp):

$$SNR_{MF}=\frac{B^2(0)}{\langle P_{NB}\rangle}=\frac{E_s f_s}{0.43\sigma^2}$$

Multiple Chirps: Coherent vs Incoherent Averaging of N_p Chirps

1) Coherent Averaging (Phase retained):

$$\langle P_N\rangle=\frac{\sigma^2}{N_p};\qquad E[B_N]=\sqrt{\frac{\pi E_s}{2f_sN_p}}\sigma$$ - Noise Background

$$Var[B_N]=0.43\frac{E_s\sigma^2}{f_sN_p}$$ - Noise Variance

$$SNR=\frac{(E_s-E[B_N])^2 f_sN_p}{0.43\sigma^2 E_s}$$

2) Incoherent Averaging (Post processing):

$$B_{av}(\tau)=B(\tau)+\frac{1}{N_p}\sum_{i=1}^{N_p}B_N(\tau)=B(\tau)+n_B$$

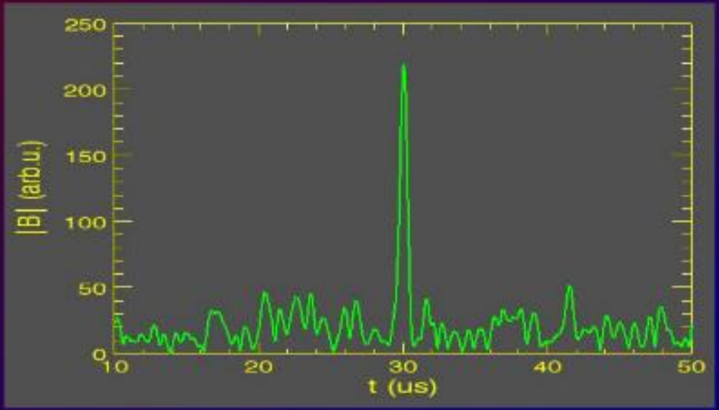
$$E[n_B]=\sqrt{\frac{\pi E_s}{2f_s}}\sigma;$$ - Independent on N_p

$$SNR=\frac{\left(E_s-\sqrt{\frac{\pi E_s}{2f_s}}\sigma\right)^2}{0.43\sigma^2E_s}f_sN_p$$

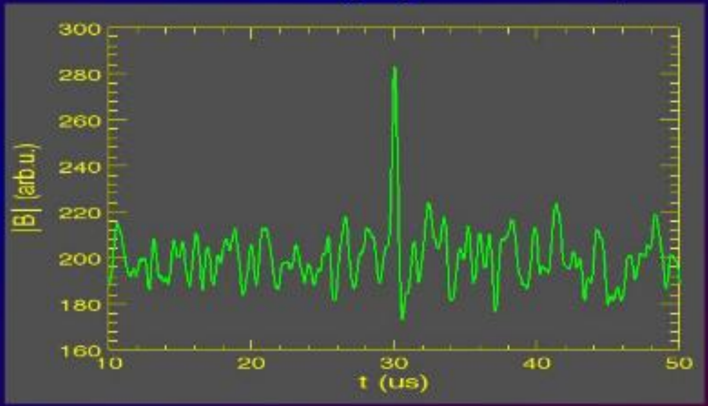
SNR of Coherent vs Incoherent Averaging

Two methods of signal detection with different level of the input noise (zero-mean Gaussian noise with std deviation σ)

Coherent Averaging of 100 chirps

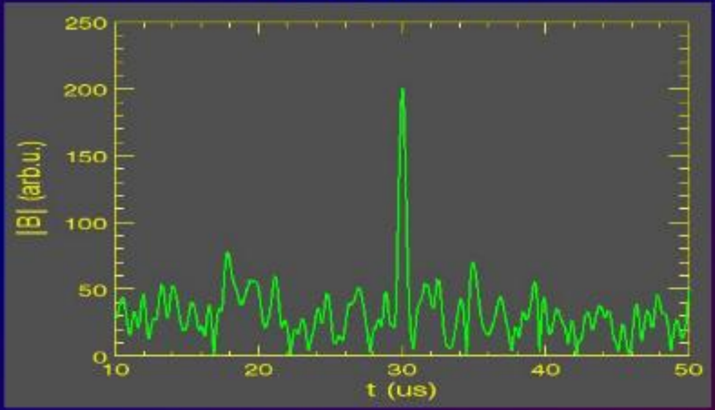


Incoherent Averaging of 100 chirps

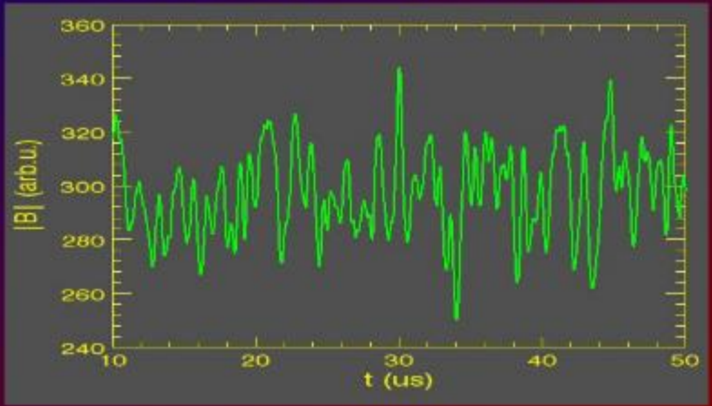


σ = 100
SNR = -23 dB

Coherent Averaging of 100 chirps



Incoherent Averaging of 100 chirps



σ = 150
SNR = -25 dB

SNR and Laser Safety Limit

Maximum Permissible Exposure (1064nm, 10-7 – 10s):

$$E_{MPE} = 5.5 \cdot T^{1/4} [J/cm^2]$$

SNR of Matched Filter Processing:

$$SNR_{MF} \sim E_s \sim A_s^2 T_{ch}$$

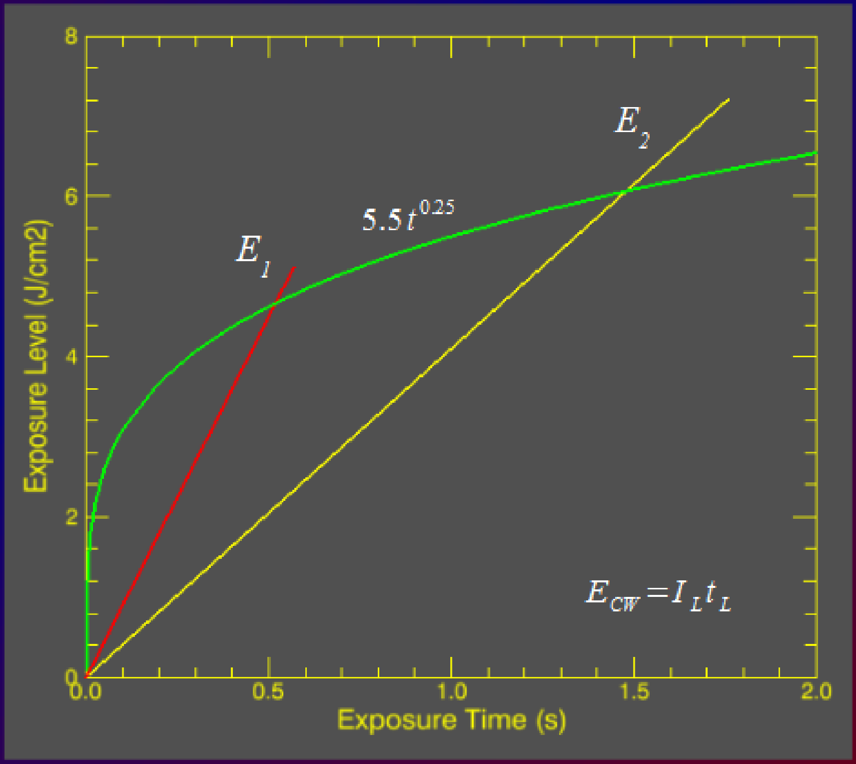
Signal Amplitude:

$A_s \sim I_L$ - Laser Irradiance [W/cm^2]

Assuming: $I_L = I_{MPE} = 5.5 \cdot T_{ch}^{-3/4}$

Then: $SNR \sim I^2_{MPE} \cdot T_{ch} \sim T_{ch}^{-1/2}$

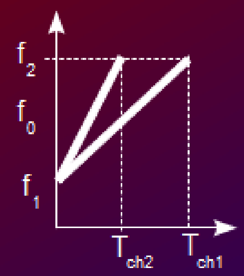
For $I = I_{MPE}$ shorter chirp duration is expected to give higher SNR



P = 1.76 W; P = 0.8 W (diam = 5 mm)

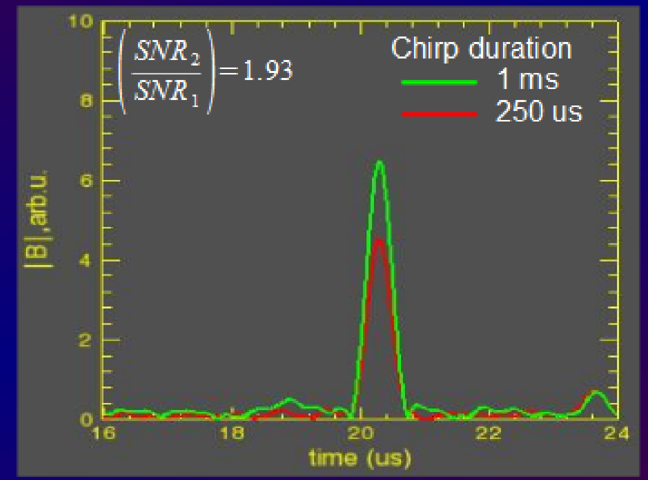
Laser safety curve

Effect of the Chirp Duration



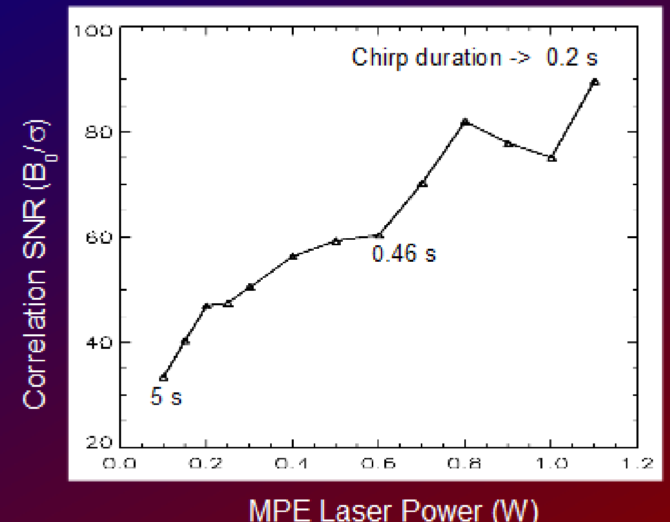
+ Gaussian Noise

Numerical Simulation using 1D Model



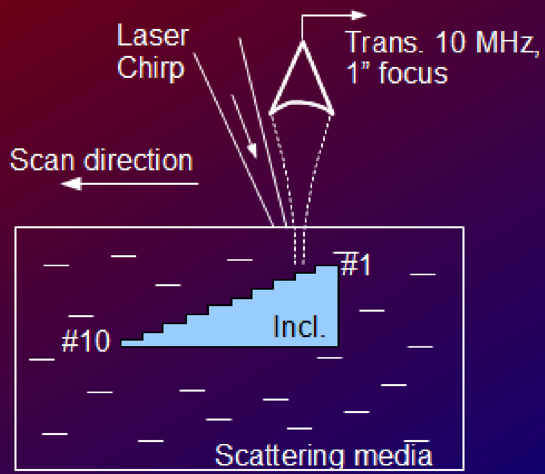
Theoretical SNR increase: $\left(\frac{SNR_2}{SNR_1}\right)=\left(\frac{T_{ch1}}{T_{ch2}}\right)^{1/2}=2$

Optical inclusion in scattering media



Predicted increase of SNR was observed in experiments with chromophores in liquid phantoms

Axial Resolution Measurements of Correlation PA

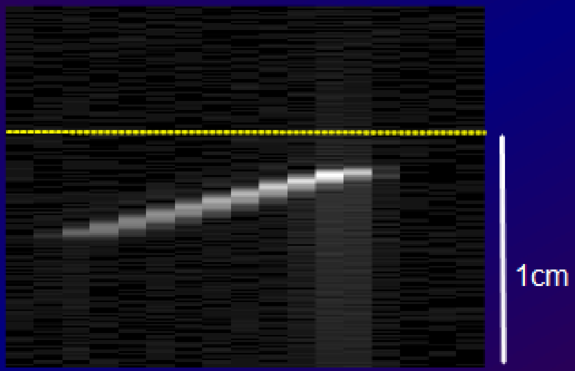


Plastic sample with 10 steps
~ 250 um height inside of
a scattering substrate

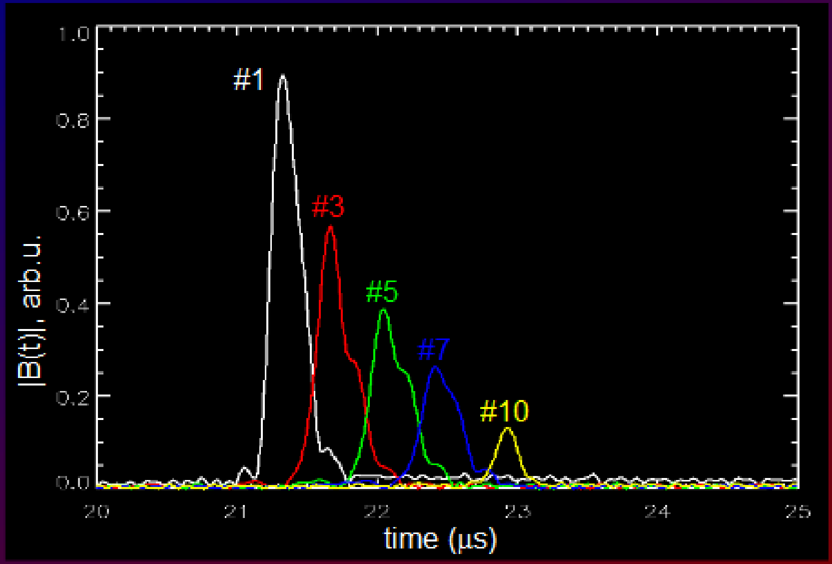
Laser chirp: 1 – 12 MHz, 1 ms

Correlation peak FWHM: ~250 ns
translates into axial resolution ~ 375 um

2D image composed of 17 A-scans



Individual A-scans

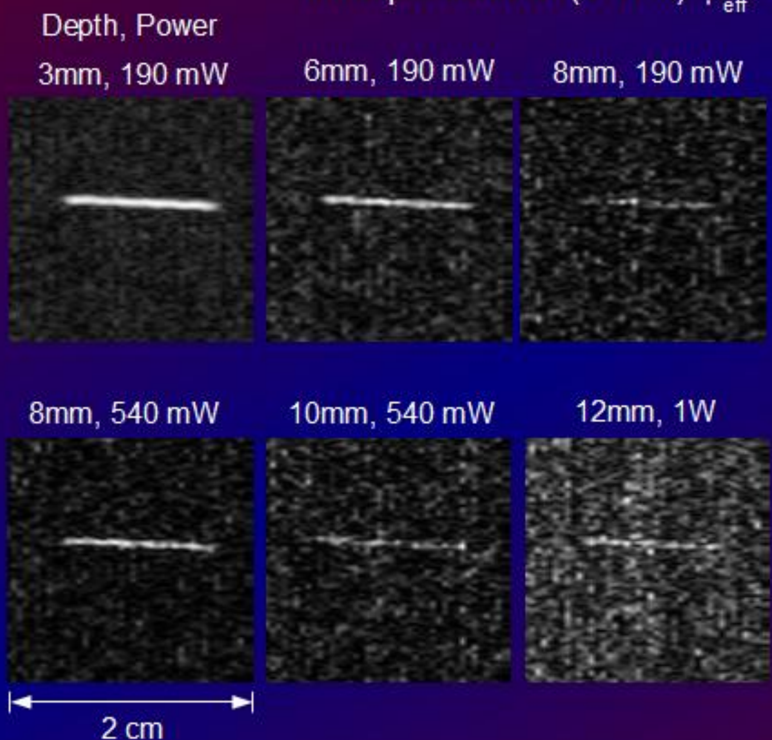


Measurements of Maximum Imaging Depth

1. Modulation chirp: 1 – 5 MHz

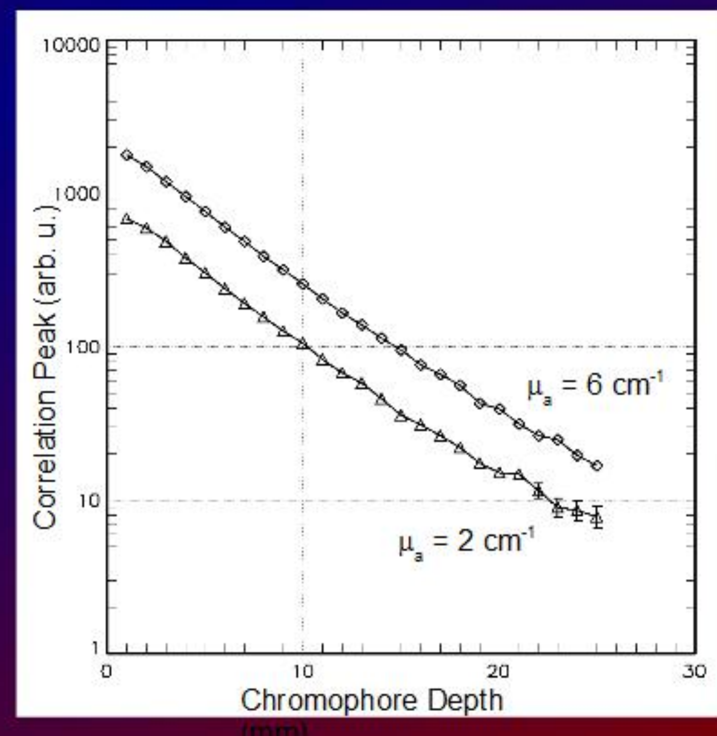
Chromophore: 12x8mm (cross section), $\mu_a = 4 cm^{-1}$
Transducer: 3.5 MHz, F = 2.54 cm, Laser spot diam =1.5 mm

Intralipid solution (0.47%): $\mu_{eff} \approx 1.3 cm^{-1}$



2. Modulation chirp: 200 – 800 kHz

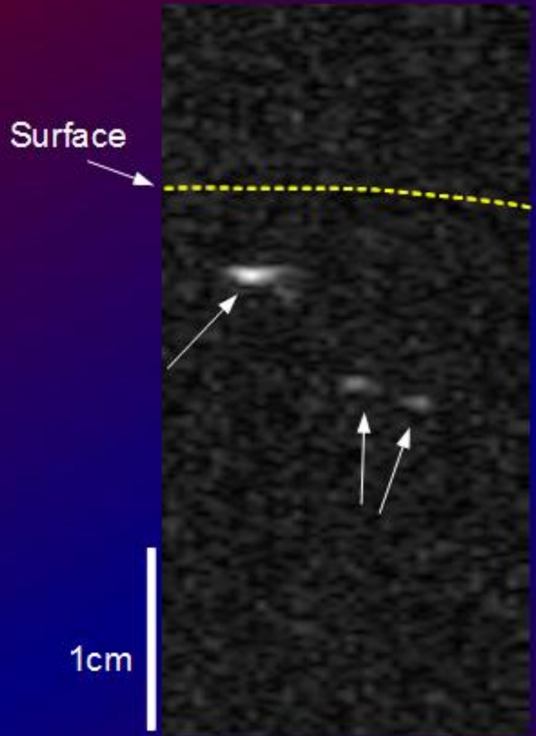
Transducer: 500 kHz, F = 5 cm



Scanning Chromophores in Tissue

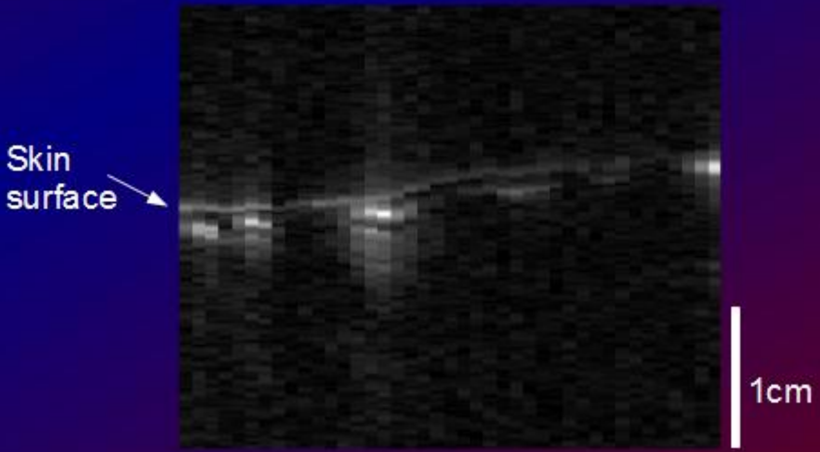
Ex-vivo muscle tissue of small animal (rat)

(Three wires inserted in muscle tissue)



Imaging of blood vessels in human wrist *in-vivo*

3.5 MHz focused transducer



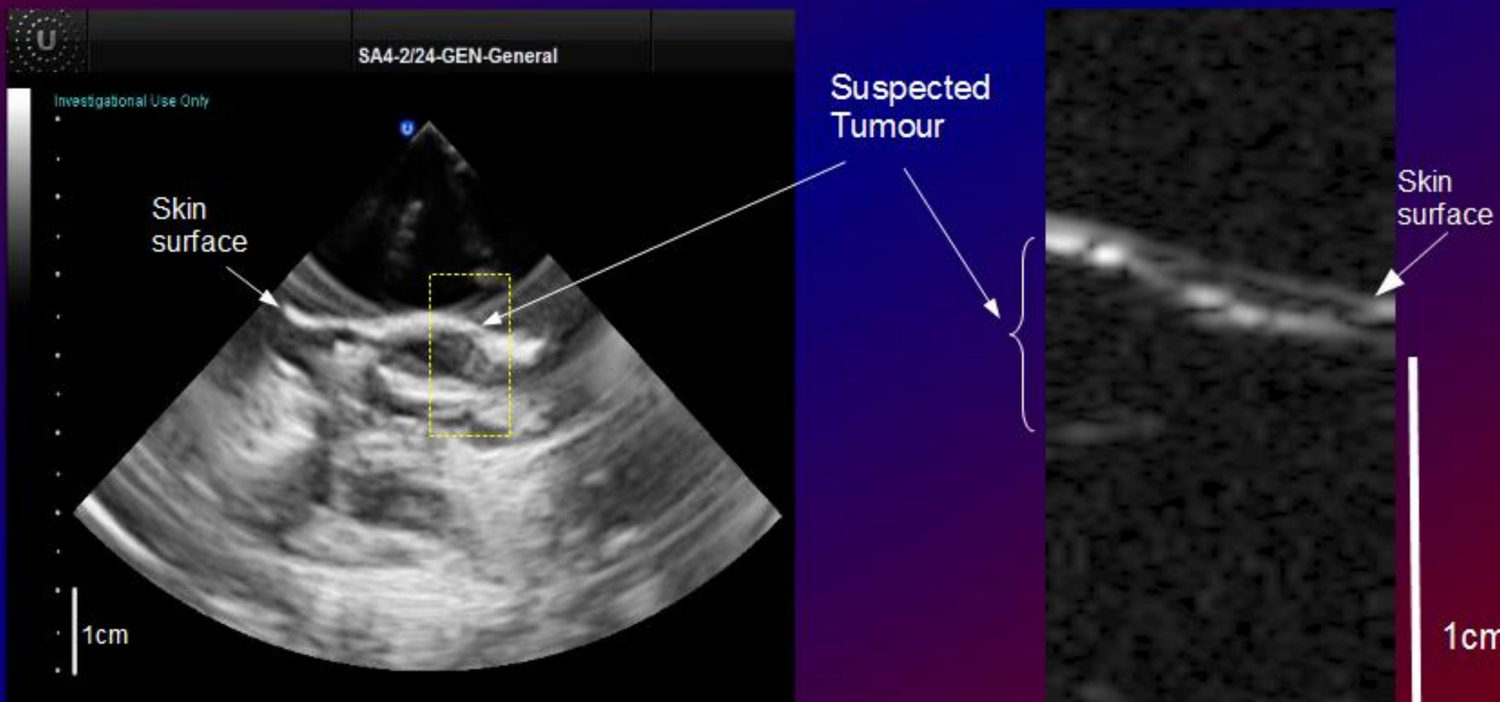
Imaging of Subcutaneous Cancer in-vivo

Tumour implanted subcutaneously in a thigh of immunodeficient rat

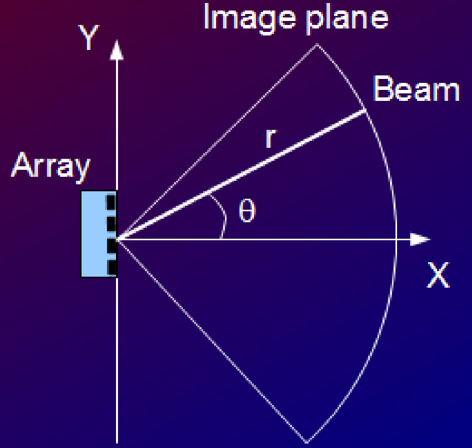
Conventional Ultrasound Image

PA Correlation Image

(Chirp: 1 – 5 MHz)



Phased Array Correlation Imaging



Correlation Phased Array – multichannel matched filter processing and beamforming in frequency domain

1) Array acquisition and FFT of signal matrix

$\tilde{B}_i(\omega) = \tilde{W}(\omega) \cdot \tilde{R}^*(\omega) \cdot \tilde{S}_i(\omega)$ - matrix N_e x N_t, N_t = 100k

2) Digital beamforming, i.e. spatial filtering by creating directional beams and beam steering

$$\tilde{U}(\omega, \theta) = \sum_{n=1}^{N_e} w_n \cdot \tilde{B}_n(\omega) \cdot \exp(-i\omega t_n(\theta)) \qquad t_n(\theta) = \frac{y_n}{c_a}\sin(\theta) + t_f$$

$$k = \frac{\omega}{c_a} = k_x^2 + k_y^2 \Rightarrow \tilde{U}(k, \theta)$$ - Spatial spectrum

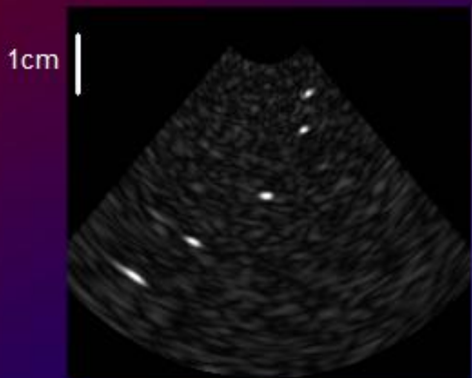
3) Backprojection:

$$u(x, y) = FFT^{-1}[\tilde{U}]$$

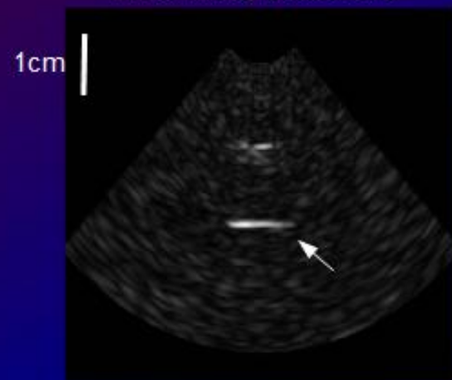
Phased array PA Correlation Imaging

Transducer phased array: 64 elements, 3.5 MHz central frequency
Laser mean power: 1W, spot diam 2.8 mm, chirp f = 1 – 5 MHz, 1ms

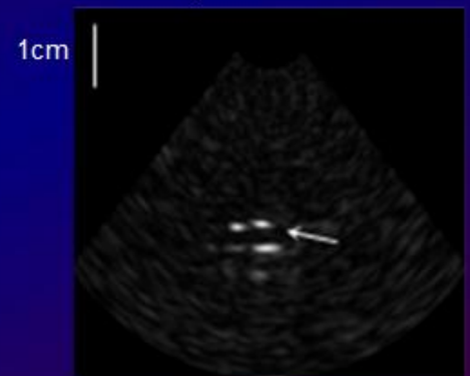
System PSF, SNR = -34dB



Optical inclusion in scattering phantom

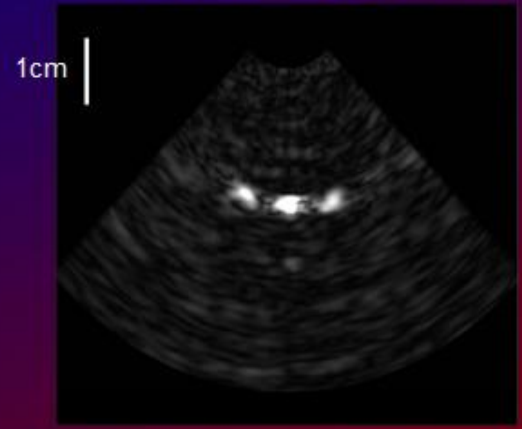


Discrete chromophores in Intralipid



Phased array probe for PA imaging

PA correlation image of wrist



Phased Array Correlation PA Imaging in-vivo

Immunodefficient rats with FaDu (carcinoma cells) injected intramuscularly

(video clip)

Day 4

(video clip)

Day 11

Laser beam (1 W, 1.5 mm in diameter) is scanned along the array axis

Conclusions

Depth-resolved PA imaging with CW laser sources is feasible using coded optical excitation (linear chirps) and correlation signal processing.

Correlation processing of coded PA response provides significant increase of SNR (> 50 dB).

Axial resolution determined by the correlation peak width can be < 300 um for the chirp bandwidth > 10 MHz.

Imaging of tissue chromophores within 2 cm depth range is feasible with inexpensive laser sources and coded modulation waveforms.

To achieve maximum SNR performance multiple chirps must be averaged coherently in pre-processing and chirp duration should be set according to MPE.

Phased array PA correlation imaging was demonstrated using conventional ultrasound array and a frequency-domain reconstruction algorithm.

Other forms of coded optical excitation including phase-coded waveforms are possible.

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