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Numerical diffusion modelling of interfering photon density waves for optical mammography

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ABSTRACT

The interference between diffusive photon density waves in turbid media was studied. A finite-difference numerical method was employed to simulate the time-dependent diffusion of photons in the red and near-infrared region. In the model the time-dispersion curves following an illumination impulse were calculated for the light transmitted through a slab geometry along a line on the distal side of the slab. The time-dispersion curves were Fourier transformed to yield the amplitude and phase as a function of modulation frequency. The interference between photon density waves was studied by having two sources, one time-delayed as compared with the other, corresponding to 180 degrees out of phase for 200 MHz modulation frequency. The diffusing waves originating from the out-of-phase sources gave as expected an amplitude null and a sharp phase transition in the mid-plane. In order to establish the model, calculated curves were compared with experimental data. Furthermore, amplitude and phase data were acquired for various objects inside the slab to study the sensitivity and robustness of the technique.

1. INTRODUCTION

Since the development of laser light sources the use of light in therapeutic and diagnostic medicine has increased rapidly. This has created a need to understand the diffusion of light in turbid media such as biological tissue.

When performing an optical transillumination for tissue diagnostics, a laser light pulse is sent through the tissue, and the transmitted light is detected^{1,2}. Usually, light in the near-IR region is used, since the tissue constituents absorb less in this wavelength region than for other wavelengths, allowing thicker tissue samples to be examined.

Light transport through a turbid (i.e. highly scattering) medium such as biological tissue can be described mathematically by the diffusion equation. This can be solved analytically for certain geometries, but for more complex geometries it has to be solved numerically. A computer code solving the diffusion equation using a finite-difference numerical method has been developed.

If a light source is intensity-modulated it launches a *photon-density wave*, which is a travelling wave of light energy density, or brightness^{3,4}. Microscopically, the photons undergo multiple scattering and the wave at optical wavelength loses coherence. Macroscopically, the photon density wave propagates with constant phase velocity at a given modulation frequency, and its phase front maintains coherence⁵. The photon-density wave is exponentially attenuated as it propagates through a turbid medium, and the attenuation and wavelength are functions of the modulation frequency and the absorption.

One method of making optical transillumination is by modulating two or more light sources so that they are 180° out of phase^{6,7,8}. If a detector is scanned along a line parallel to the laser source array, there will be an amplitude null and a sharp phase transition when the detector crosses the mid plane between the in- and anti-phase sources. If there is an absorbing region (e.g. a tumour) in the sample, and this absorber is scanned with respect to the sources-detector arrangement, there will be a 180° phase shift when it crosses the mid plane. With this method, even very small absorbers can be detected inside a turbid medium, and hopefully it can be used to find very small tumours in the female breast.

In this paper, results from numerical simulations have been used to investigate this method. The case of a homogeneous medium has been simulated as well as a medium containing an absorbing region, and the results have been verified by experimental results. The case of an inhomogeneous medium, with many small absorbers has also been investigated.

2. SIMULATIONS

2.1. Theory

A mathematical description of the propagation and scattering characteristics of light in a turbid medium can be made in different ways⁹:

- *Analytical theory*, where we start with Maxwell's equations and take into account the statistical nature of the medium and of the wave. This is the most fundamental approach, but mathematically it is very complex.
- *Transport theory*, which deals directly with the transport of power through the medium, instead of starting with Maxwell's equations. In this model coherent optical effects such as diffraction and interference are neglected as well as inelastic scattering (e.g. fluorescence).
- *Monte Carlo simulations* is a method based on tracing a large number of light rays entering the tissue. The scattering events within the tissue are determined by a probability function matching the scattering coefficient. At each scattering a part of the ray, determined by the absorption coefficient, is absorbed. The scattering angle is given by the scattering phase function.

In this paper, the transport theory has been used. The linear transport equation (Boltzmann Equation) is a balance equation describing the flow of particles (e.g. photons) in a given volume element under consideration of their velocity, location and changes due to collisions (i.e. scattering and absorption).

The transport equation in its general form is impossible to solve. However, in some cases it is possible to approximate the light transport with the diffusion equation. This approximation gives an accurate prediction of the light distribution after many scattering events provided that:

- The scattering dominates over the absorption;

$$\mu_a \ll (1-g) \mu_s$$

where μ_a is the absorption coefficient, μ_s the scattering coefficient and g the anisotropy factor which is the mean cosine of the scattering angle.

- Detection is made far from the light sources (so that we can assume multiple scattering)

As for the first condition, scattering generally dominates over the absorption in soft tissues for wavelengths between 650 and 1300 nm. If we assume that the conditions are fulfilled, the diffusion approximation can be made and the transport equation is simplified to yield the *diffusion equation*:

$$\frac{1}{c} \cdot \frac{\partial}{\partial t} \phi(\mathbf{r}, t) - D \nabla^2 \phi(\mathbf{r}, t) + \mu_a \phi(\mathbf{r}, t) = q(\mathbf{r}, t) \quad (1)$$

where $\phi(\mathbf{r}, t)$ is the diffuse fluence rate, $q(\mathbf{r}, t)$ is the photon source and D is the diffusion coefficient, $D = [3(\mu_a + (1-g)\mu_s)]^{-1}$. This equation can be solved analytically for some simple geometries. For a homogeneous tissue slab it has been solved by Patterson *et al.*¹⁰ to

$$T(d, t) = (4\pi Dc)^{-1/2} t^{-3/2} \exp(-\mu_a ct) \times \left\{ (d - z_0) \exp\left[-\frac{(d - z_0)^2}{4Dct}\right] - (d + z_0) \exp\left[-\frac{(d + z_0)^2}{4Dct}\right] \right. \\ \left. + (3d - z_0) \exp\left[-\frac{(3d - z_0)^2}{4Dct}\right] - (3d + z_0) \exp\left[-\frac{(3d + z_0)^2}{4Dct}\right] \right\} \quad (2)$$

where d is the slab thickness and $z_0 = [(1-g)\mu_s]^{-1}$.

Since we want to study inhomogeneous slabs of tissue, a computer code solving the diffusion equation numerically has been used. This allows us to have regions with differing scattering and absorption inside the slab.

2.2. The ADI-algorithm

When the diffusion equation is translated to a differential equation for finite room- and time steps, a tridiagonal system of equations is yielded. This is solved by the computer by using a generalized Crank-Nicholson algorithm in three dimensions called the ADI (alternating direction implicit)

method¹¹. It solves the equation for each dimension separately using a third of a time-step for the x, y and z variables. The resulting equation for the x dimension is:

$$\begin{aligned} \phi_{xyz}^{t+1/3} - \phi_{xyz}^t = \frac{c\Delta t}{3n\Delta^2} \{ & D_{x+1/2yz}(\phi_{x+1yz}^{t+1/3} - \phi_{xyz}^{t+1/3}) - D_{x-1/2yz}(\phi_{xyz}^{t+1/3} - \phi_{x-1yz}^{t+1/3}) \\ & + D_{xy+1/2z}(\phi_{xy+1z}^t - \phi_{xyz}^t) - D_{xy-1/2z}(\phi_{xyz}^t - \phi_{xy-1z}^t) \\ & + D_{xyz+1/2}(\phi_{xyz+1}^t - \phi_{xyz}^t) - D_{xyz-1/2}(\phi_{xyz}^t - \phi_{xyz-1}^t) \} - \frac{c\Delta t}{6n} \mu_a (\phi_{xyz}^t - \phi_{xyz}^{t+1/3}) \end{aligned} \quad (3)$$

where ϕ_{xyz}^t is the fluence rate in the matrix element (x,y,z) at time t, Δt is the time step, Δ is the step size in x, y and z directions and $D_{x+1/2yz}$ is the average of the diffusion coefficient in the matrix elements (x,y,z) and (x+1,y,z).

The slab of tissue was described by a 3-dimensional matrix with cubic elements. In this case, the side of an element, dx, was set to 2 mm. The model is described in figure 1.

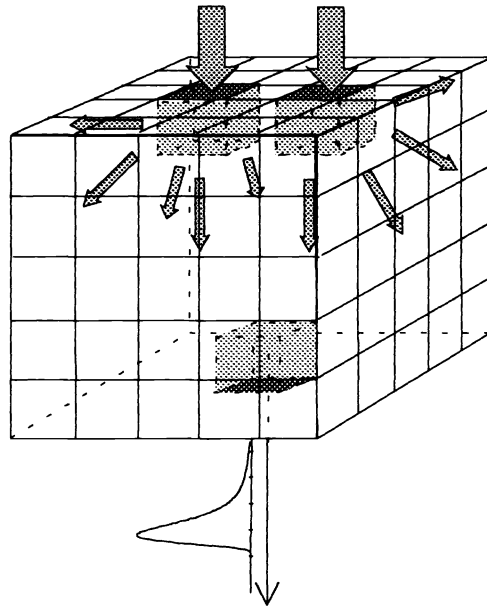


Figure 1. The tissue sample is simulated by a lattice with cubic elements. Two of the elements are given non-zero values for a duration Δt , to simulate incident light pulses. In each detector element, the whole time dispersion curve is recorded.

In the simulations, the matrix had $75 \times 50 \times 17$ elements, corresponding to $150 \times 100 \times 34$ mm. The scattering and absorption coefficients are set uniformly throughout the sample, except for in an arbitrary number of regions, where the optical properties can be set separately. Here, μ_a and μ_s' were set to 1.7 and 2400 m^{-1} , respectively, and in the absorbing region μ_a was set to 10000 m^{-1} while μ_s' remained the same. The boundary elements in the x- and y-direction were set to the value of its

nearest neighbour inside the matrix, whereas the photon densities in the boundary elements in the z -direction were set to zero. Patterson *et al.* have shown that this simplification is adequate when only the phase and modulation are studied, since these depend on the pulse shape and not on the pulse amplitude¹⁰.

To simulate the incident light pulses, the voxels where the sources are situated are set to a non-zero value (representing the light intensity) for one time interval, Δt , which was 12 picoseconds.

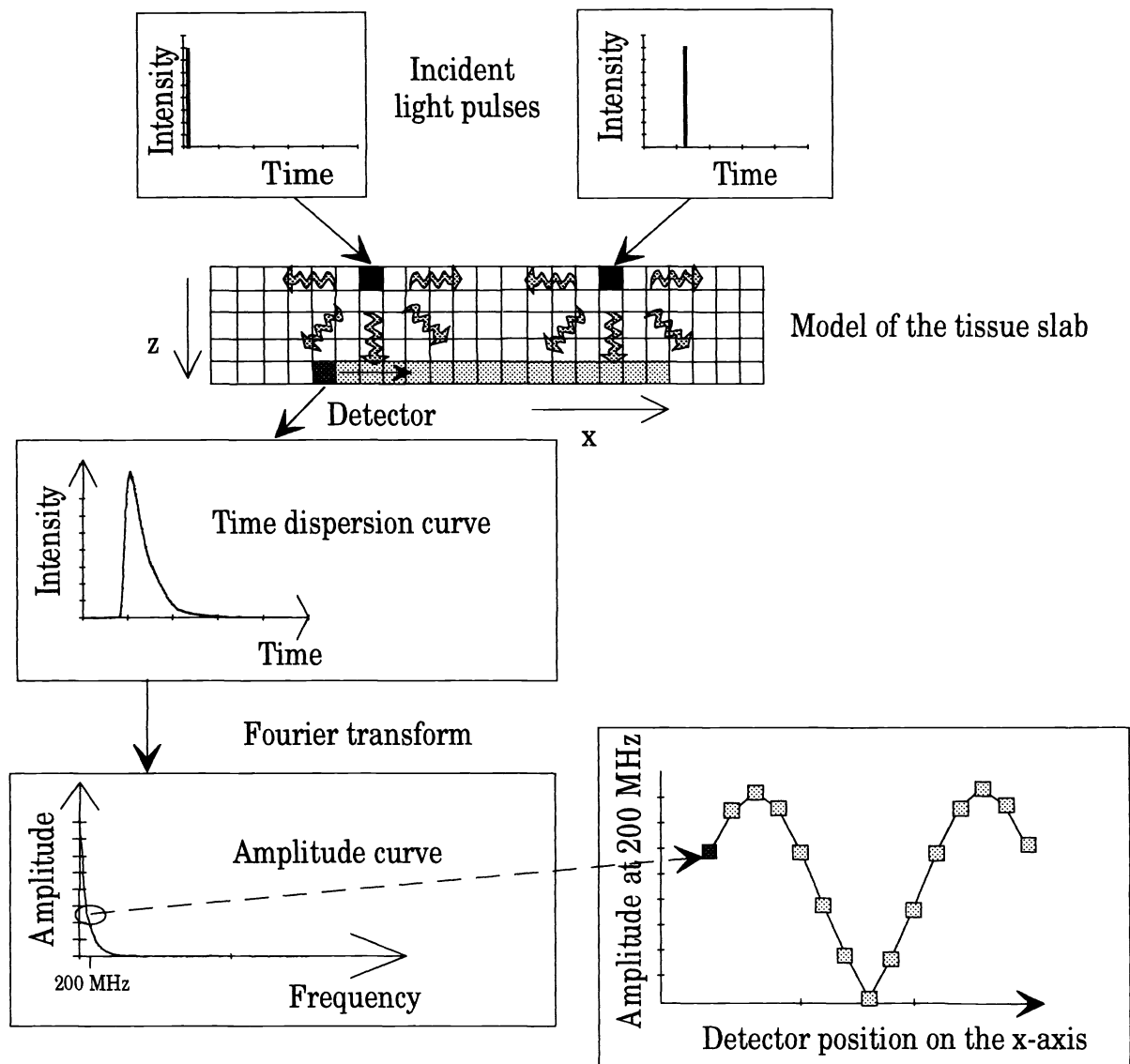


Figure 2. Short light pulses diffuse through the sample, and the resulting time dispersion curves in different detection points are recorded and Fourier transformed. The values of phase and amplitude at the modulation frequency 200 MHz are extracted in each detection point, and these values form the amplitude-dip and phase-shift curves.

To simulate the phase shift between the two sources, a time delay between the two source pulses is used. This time delay is chosen so that it corresponds to a 180° phase shift at the chosen modulation frequency. In these experiments, the modulation frequency was 200 MHz, and the corresponding time delay between the pulses from the two sources is thus 2.5 nanoseconds.

The diffusion of light through the sample is simulated and the resulting light intensities in the chosen detector pixels are saved for each time interval, Δt . The detected time dispersion curves are then Fourier transformed to yield the amplitude- and phase curves. See figure 2. Frequencies down to $1/(n \Delta t)$ where n is the number of iterations and Δt the time step can be resolved. To get a good enough resolution, Δt and n must be large enough. In this case, Δt was 12 ps, and thus n should be at least 2048 or 4096 to ensure good resolution of the modulation frequency, 200 MHz. In this study, n was set to 2048.

3. EXPERIMENTS

All results presented in this paper were obtained in a transmission geometry. The tissue model consisted of a 150 *100 mm block of Delrin plastic. The optical properties were estimated to $\mu_s'=2400 \text{ m}^{-1}$ and $\mu_a=1.7 \text{ m}^{-1}$ by doing a fit to the solution to equation (1). To simulate a tumour inside the tissue, a block with a cylindrical hole containing charcoal was used. The diameter of the hole was 5 mm, and it was situated on maximum depth and along the y-axis.

In the homogeneous case, the sources and the sample were fix whereas the detector was scanned along the x-axis on the distal side of the sample. In the inhomogeneous case, the sources and the detector were fix, and the sample was scanned (corresponding to scanning a source-detector unit along the sample). The light source was a Ti:S laser operating at 790 nm with 100 fs long pulses. In this case we are initially working in the time-plane and the 180° phase shift is obtained by sending the two light pulses at a time separation that corresponds to half the wavelength. Note that this wavelength is not the light wavelength, but the wavelength corresponding to the chosen modulation frequency. The sources were in this case modulated at a frequency of 200 MHz, corresponding to a time separation between the two light pulses of 2.5 nanoseconds.

4. SIMULATED AND EXPERIMENTAL RESULTS

As described in the previous section, these experiments were conducted in a transmission geometry, with two out-of-phase sources and one detector.

4.1. Homogeneous sample

Initially, the sample was homogeneous, without any absorbing region, and the detector was scanned along the x-axis on the distal side of the sample. The spacing between the sources was approximately 30 mm, and the sample was 34 mm thick.

In the simulations, the 0° source was located at $x=30$, corresponding to 60 mm ($dX = 2 \text{ mm}$). The 180° source was at $x=46$, corresponding to 92 mm. Hence, there is an amplitude null and a sharp

phase transition at $x = 38$ (76 mm). The optical constants μ_a and μ_s' were set to 1.7 and 2400 m^{-1} , respectively. Results are shown in figure 3. When comparing the simulated values with the experimental ones, we can see that they agree well.

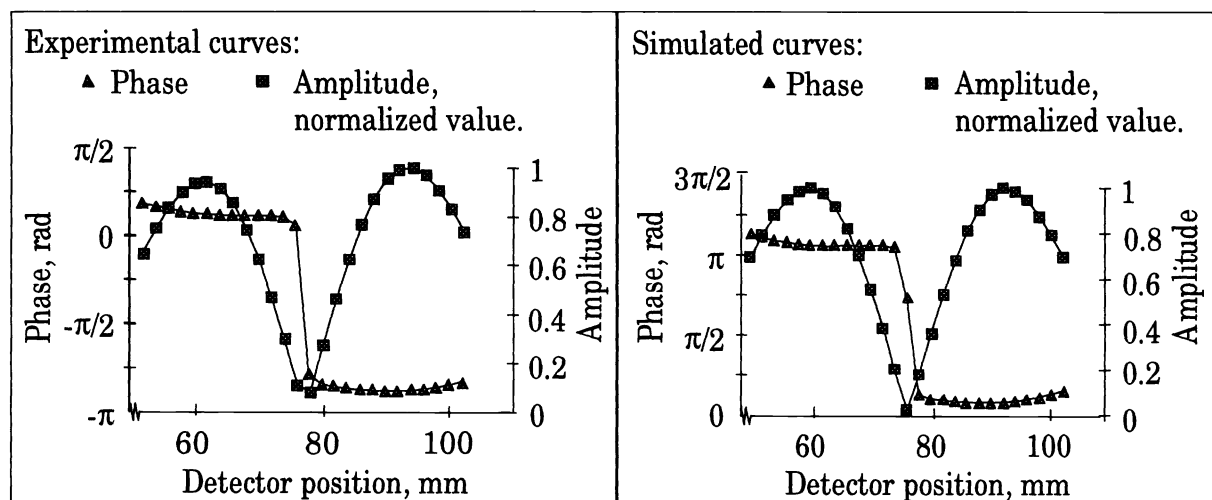


Figure 3. Amplitude and phase values received from experiment and simulation of a homogeneous tissue slab.

4.2. Sample containing an absorber

In the second test, an absorbing region has been scanned inside the sample in the x -direction. This is equivalent to scanning sources and detector in parallel across the sample. The absorbing region is supposed to mimic a tumour. In this case, the absorber was cylindrical with the diameter 5 mm, and the Delrin block was 42 mm thick.

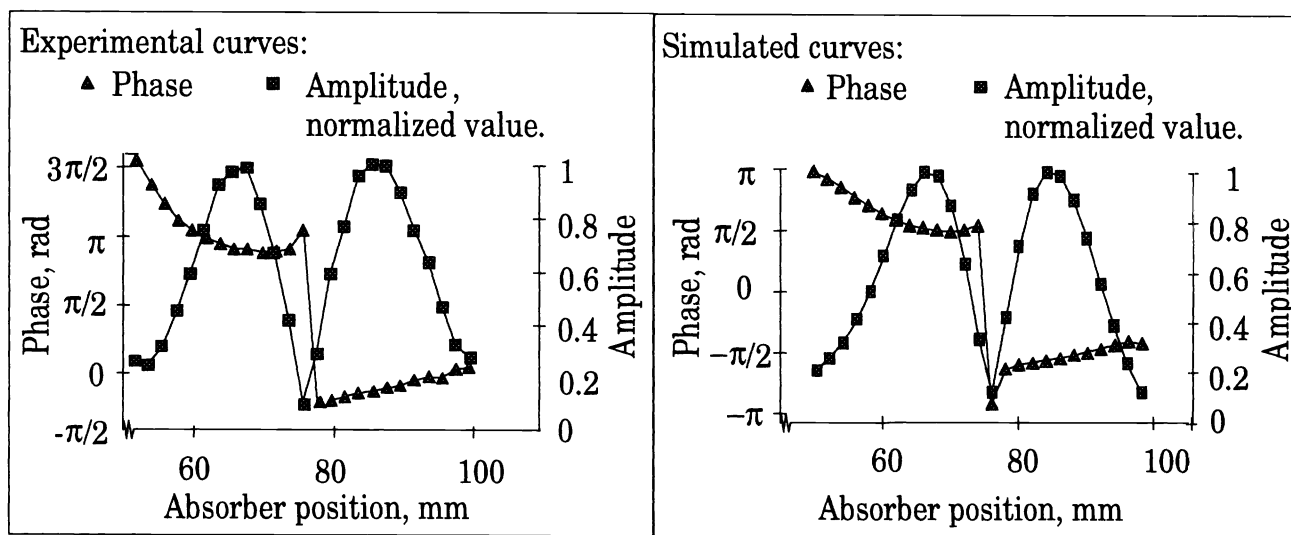


Figure 4. Amplitude and phase plots when scanning an absorbing cylinder inside the sample.

If we study the resulting amplitude and phase curves in figure 4, we see that their shapes are similar to the experimental ones.

4.3. Inhomogeneous sample, simulations

It is of interest to find out how well this method works if the sample contains many small inhomogeneities. This was investigated by making simulations of samples containing many small absorbers, one voxel each, at random places.

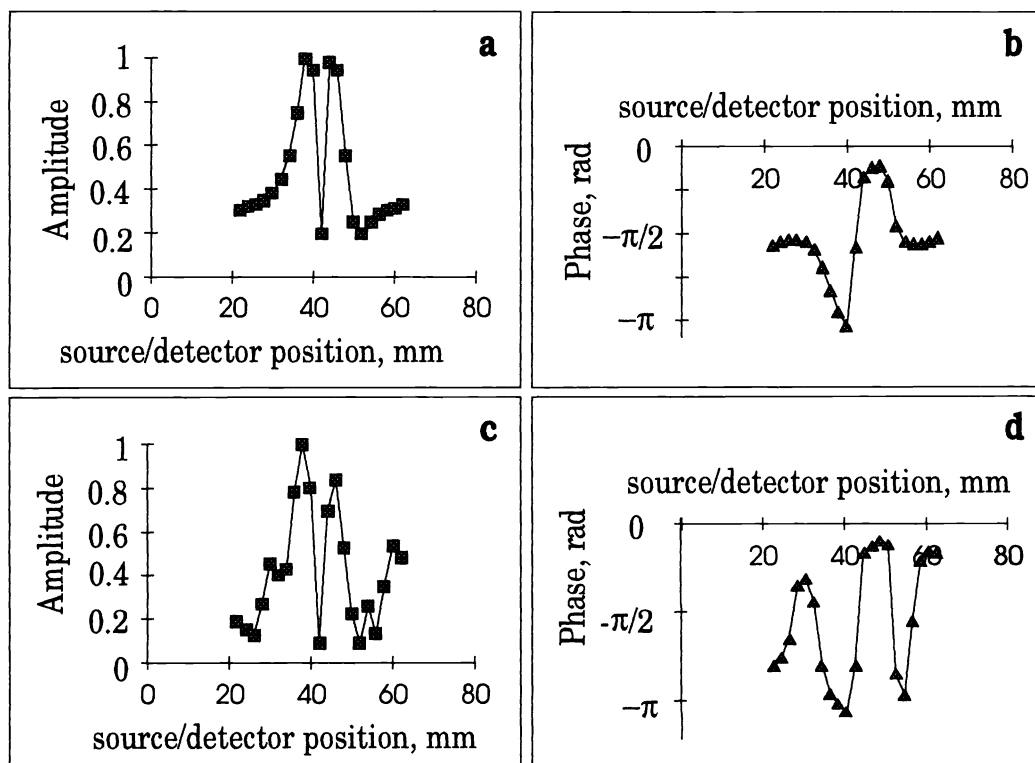


Figure 5. In a and b, the sources and the detector have been translated through a sample with only one, large, absorber (same type of simulation as in figure 4). Figure 5a shows amplitude versus absorber position and 5b shows phase. 5c and 5d show the amplitude and phase for the same type of measurement, but in addition to the large absorber there are 100 small (voxel sized) absorbers in arbitrary positions inside the sample.

The features of the a and b curves can still be seen in c and d, but they seem to be disturbed. In d, for example, there is a large shift at $x = 32$. One reason might be that many small absorbers have gathered around that value, and that they affect the phase as one large absorber would have done. However, further studies are required to be able to draw any reliable conclusions.

5. DISCUSSION AND CONCLUSIONS

This work has clearly shown that the developed computer code well manages to simulate transillumination experiments. When simulations are made of interfering diffusive waves from two light sources, and the resulting time dispersion curve is Fourier transformed, the amplitude- and phase- curves agree very well with those obtained from experiments. Similar results have previously been obtained by Knüttel *et al.* as well as by Kang, Chance *et al.* This paper confirms that the spatial resolution is very high in the case of a homogeneous medium. Kang and Chance have also examined the problems arising when two absorbers are to be resolved⁷. This work has shown that the more common case with an inhomogeneous medium also might be difficult. However, further studies are necessary to draw any firm conclusions and to evaluate how useful this method can be for *in vivo* studies of breast tissue.

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