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SPECIAL REPORT

Feasibility of intracranial near-infrared optical scanning

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Abstract

Light injected at a point on a surface of a scattering medium is emitted at the surface after traveling a quasi-semicircular path deep into the medium. This phenomenon can be exploited to detect objects immersed in the medium from time-resolved measurements of light intensity at the surface. Our experiments on model systems demonstrate that absorbing objects, surrounded by bone and other scattering material, can be detected. The technique yields surface images of absorbing objects submerged in a scattering medium. Images of the same phantoms inside the cavity of a skull can be obtained by the same technique.

Descriptors: Noninvasive functional brain imaging, Photon migration in tissues

Functional images of internal body structures are important investigative and clinical tools in physiology and medicine. Recently, they have attracted considerable attention in neuroscience (e.g., LaBerge, 1990; Petersen, Fox, Posner, Mintun, & Raichle, 1988). Techniques based on scanning body tissues with nonionizing electromagnetic radiation of near-infrared wavelengths have been proposed as tools for in vivo metabolic imaging of brain activity because of their potential low cost, good spatial resolution, noninvasive nature, and near real-time response (Arrige, Cope, & Delpy, 1992; Benaron & Stevenson, 1993; Chance, 1989, 1991; Kato, Kamei, Takashima, & Ozaki, 1993). These techniques exploit changes that occur in the optical properties of particular areas of the brain that correlate with changes in metabolic activity and/or hemodynamics. Grinvald, Lieke, Frostin, Gilbert, and Torsten (1986) used visible light to detect variations of the reflectivity of localized brain surfaces. Their method applied to changes at the surface of the brain and required the removal of portions of the skull. Our data show that it is possible to obtain optical images of absorbing structures inside a skull from measurements taken from the skull's surface. The experiments suggest that brain-surface reflectivity/absorption measurements may be possible without surgery by using noninvasive optical methods.

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Photon Migration in Scattering Media

In homogenous and infinite scattering media, photons follow a random path. In surface-bound media some of the photons reach the surface, exit from the medium, and, if the surface is flat or convex, do not reenter the medium. This creates a distortion in the photon density. If the light source is located on the surface of a homogenous, semi-infinite medium, the photon density can be modeled with the same equations that describe the positive half of a dipole field (Farrell, Patterson, & Wilson, 1992). The average path followed by the photons follows the force lines of this field. An absorbing object located deep in the medium intercepts some of these photons. Scattering objects also produce deformations of the photon density field and therefore can be detected. This absorption of light results in a shadow of the object on the same surface that has been illuminated.

Figure 1 illustrates the expected effect of an absorbing object on the light reaching the surface of the medium. Changes in the amount of light reaching the detector also can be due to local variations in the scattering properties of the medium. Images of the average intensity of the light reaching the surface of the

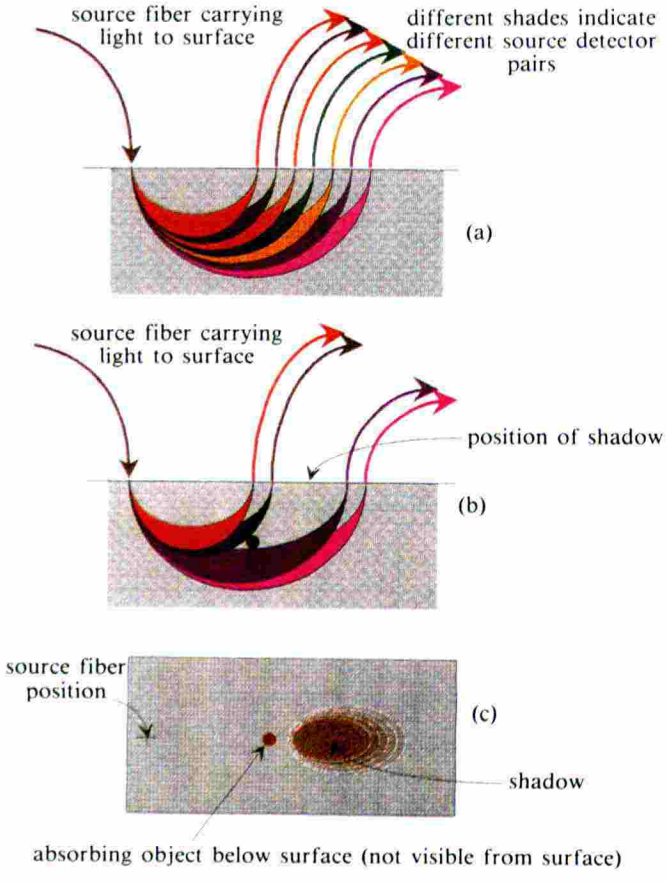

Figure 1. Schematic illustration of the diffusion of light through a semi-infinite scattering medium. When the light is applied through a point on the surface of the medium, the photons travel independently in random paths. Because photons that pass across the surface leave the system and therefore can never get to the detector, the presence of the surface "causes" the photons that travel from the source to the detector to move, on average, within the crescents indicated by the shaded colored shapes. (a, view from side) Each source-detector pair selects a different set of photon paths: the larger the separation, the deeper the penetration. (b, view from side) When an absorbing object is placed beneath the surface, it deletes photon paths (deleted paths not shown), yielding a shadow on the surface. (c) View from the surface of the shadow caused by an absorbing object.

medium do not discriminate between the effects of absorbing or scattering objects. However, absorbing and scattering objects do produce different effects on the time photons take to travel from the source to the detector ("time of flight"; Sevick, Chance, Leigh, Nioka, & Maris, 1991). For this reason, time-resolved (Sevick et al., 1991) and, more recently, frequency-domain optical techniques (Mantulin, Fishkin, So, Gratton, & Maier, 1993) have been introduced to determine separately the absorption and scattering properties of scattering media.

The physical considerations that are at the basis of frequency-domain optical imaging, the instrumentation as well as the details of the specific algorithms used have been described elsewhere (Gratton et al., 1990; Maier & Gratton, 1993). Briefly, the technique involves passing monochromatic light, which is intensity-modulated at a radio frequency (10–300 MHz), through body tissues and observing the variations in (a) the average amount of light reaching the detector (*d.c. intensity*), (b) the phase delay determined by the tissue (measured by the *phase* between the input and output signals), and (c) the *modulation* of the photon density wave (measured by the ratio between the a.c. to d.c. contribution). These parameters are determined by the absorption (m_a) and scattering (m_s) properties of the sample volume through which the injected photons travel before reaching the detector. Using detectors at different points on the surface to measure these parameters provides a surface map useful in the study of objects submerged inside the scattering medium. Previous studies showed that the technique has potentially high spatial resolution (Maier & Gratton, 1993). Images of objects as small as a fraction of a millimeter can be rapidly obtained in less than a millisecond in scattering media when the scattering and absorption coefficients are similar to various tissues (e.g., brain tissue). In this paper we report data from three experiments that show that measurements of photon migration parameters can yield images of structures inside the skull.

Experiment 1

Interpretation of a surface map of d.c., phase, and modulation requires knowledge about the average photon trajectories between the source and the detector. Any object along the photon path will cause changes in the light that reaches the detector. Given the random diffusion process, there is a theoretically infinite number of different paths between the source and the detector. However, some paths are more likely than others, generating a probability distribution for different paths. In addition to providing important cues for three-dimensional reconstruction, knowledge about the path distribution may help in understanding what limits of penetration and resolution can be reached by the technique. In this experiment we measured the distribution of paths the light follows between a particular source-detector pair.

Methods

A semi-infinite scattering medium was approximated by a tank (dimensions: 40 cm long, 30 cm wide, 15 cm deep) full of skim milk ($m_a \simeq 0.002$/mm, $m_s \simeq 0.5$/mm—note that these values are close to those of most living tissues, where is $m_a \simeq 0.001$–0.01/mm and $m_s \simeq 0.5$–10/mm). Our source, a diode laser (intensity 0.5 mW), was used to produce 800-nm light intensity modulated at 120 MHz. The only light in the system was introduced by our source. The light reaching the detector was measured with a frequency-domain spectrometer (Maier & Gratton, 1993). A cross-correlation frequency of 100 Hz was added to allow measurements of the light phase and modulation (Gratton et al., 1990). The light was conveyed to, and picked up from, the milk surface by fiber-optic cables. The measurement was obtained by fixing the locations of the source and detector fibers separated by 72 mm on the surface of the milk (indicated by the arrows in Figure 2), and moving a small (3-mm diameter) absorbing sphere ($m_a > 1{,}000$/mm) below the surface in 2-mm steps. Motion of the probe sphere was in the plane perpendicular to the surface of the milk, containing the source and detector. A different measurement of the light reaching the detector was obtained for each position of the sphere, providing a map of how different absorber positions affect surface measurement.

Results

Figure 2 presents changes in d.c. intensity (left panel), phase (middle panel), and modulation (right panel) of the light reach-

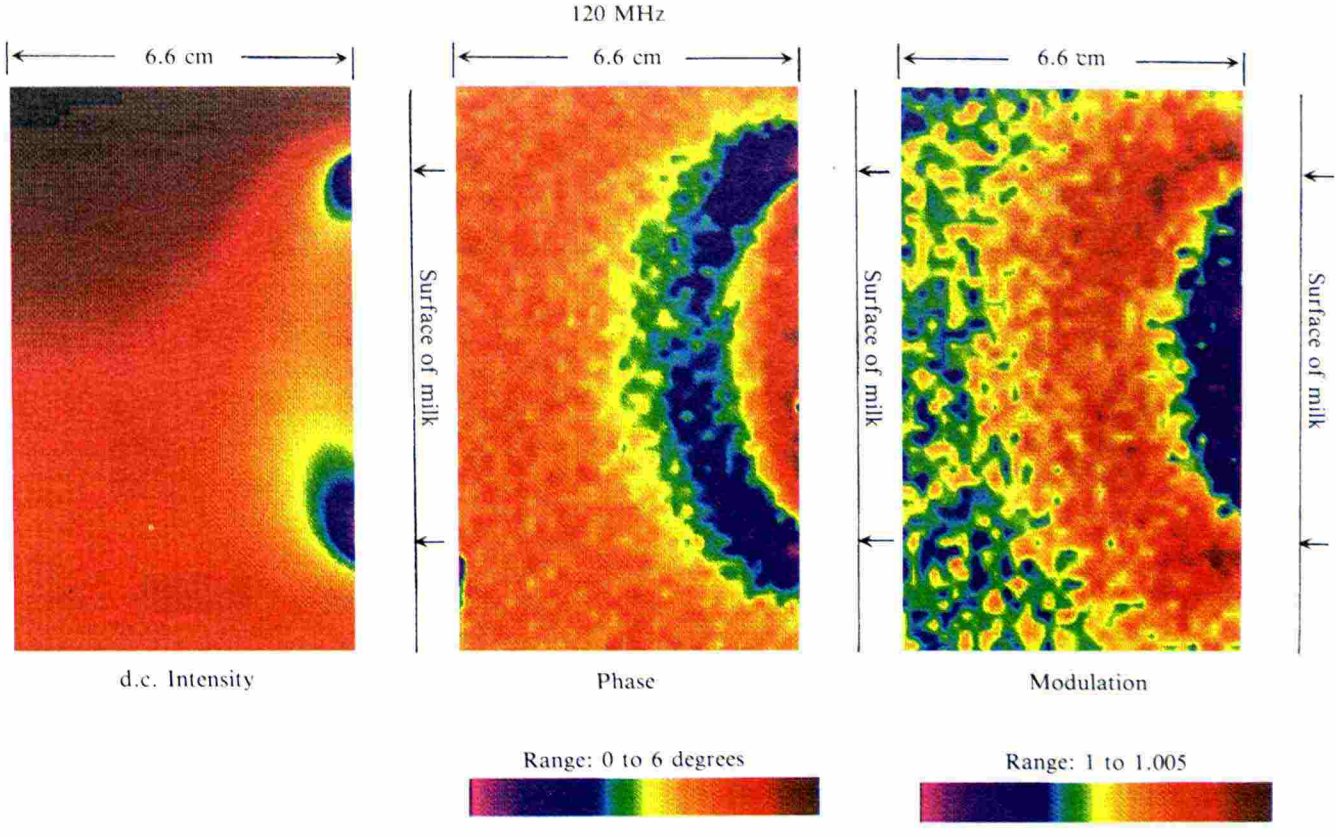

Figure 2. Experimental measurement of the path followed by photons emitted by a point located on the surface of a quasi-semi-infinite scattering medium and reaching a particular location on the same surface. The arrows indicate the locations of the source and the detector.

ing the detector fiber as a function of placement of the sphere. The data reported in this figure indicate that, in a surface-bound scattering medium, the distribution of the light paths between a source–detector pair located on the surface has a crescent shape, with a cross-section that is larger in the middle and narrower near source and detector. For a distance of 72 mm between the source and the detector, the paths reach an average depth of about 20 mm. This approximation can be used as an initial estimate of the penetration depth of the technique. Note, however, that, given that the path is distributed, objects that are deeper than the average path depth can still exert an effect on the surface measurements.

Experiment 2

The data reported in Figure 2 show that absorbing objects located beneath the surface of a scattering medium produce measurable effects at the surface of the medium when a point on the surface is illuminated. In Experiment 2 we obtained an image of the surface shadow of a deep object.

Methods

The light source was a light-emitting diode (HP1404). An absorbing sphere ($r = 7$ mm) was submerged below the surface of a scattering medium (skim milk). The sphere was not visible with the naked eye from the surface of the medium. The source and detector, separated by a distance of 72 mm, were moved in tandem, scanning the surface in steps of 5 mm, and measurements of d.c. intensity, phase, and modulation were taken for each position. The rest of the apparatus was the same as that used in Experiment 1.

Results

In Figure 3 we show the surface image obtained with this method. It shows that an object below the surface of a scattering material, although not visible with the naked eye, can be detected through time-resolved light-intensity measurements made with a source–detector pair scanning across the surface. The ball appears elongated because of the shape of the bundle that is sampling it.

Experiment 3

The measurements reported previously were collected with a homogenous medium. However, the human head clearly is not homogenous. This lack of homogeneity will result in distortions of the images, so that the actual data obtained in intact preparations may not be as clearly interpretable as those obtained in a homogeneous medium. In particular, the skull and other bony structures may introduce significant departures from homogeneity. To test whether it is possible to derive interpretable images in a more complex situation, we performed an experiment in which we derived the image of a sphere contained in a sheep skull submerged in a scattering medium.

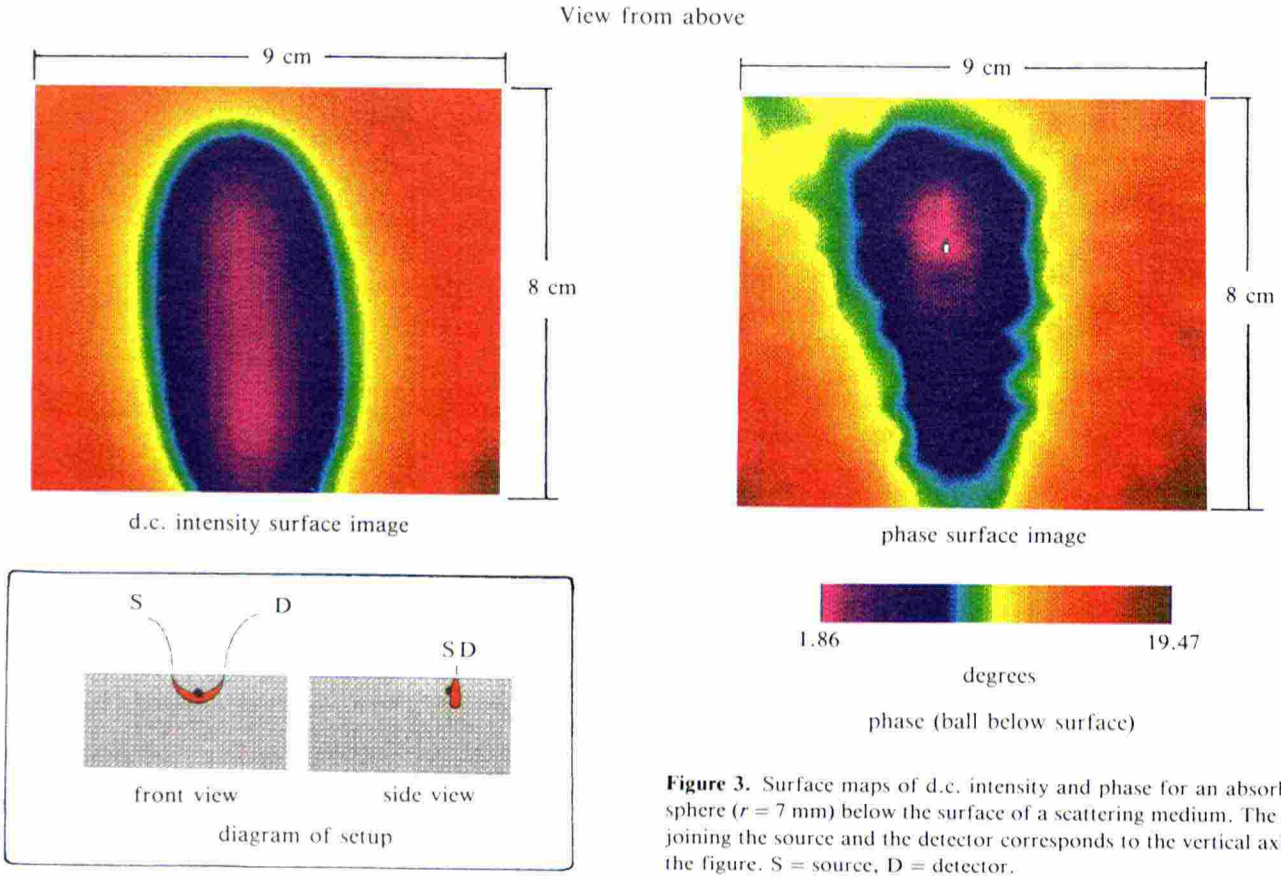

Figure 3. Surface maps of d.c. intensity and phase for an absorbing sphere ($r = 7$ mm) below the surface of a scattering medium. The axis joining the source and the detector corresponds to the vertical axis in the figure. S = source, D = detector.

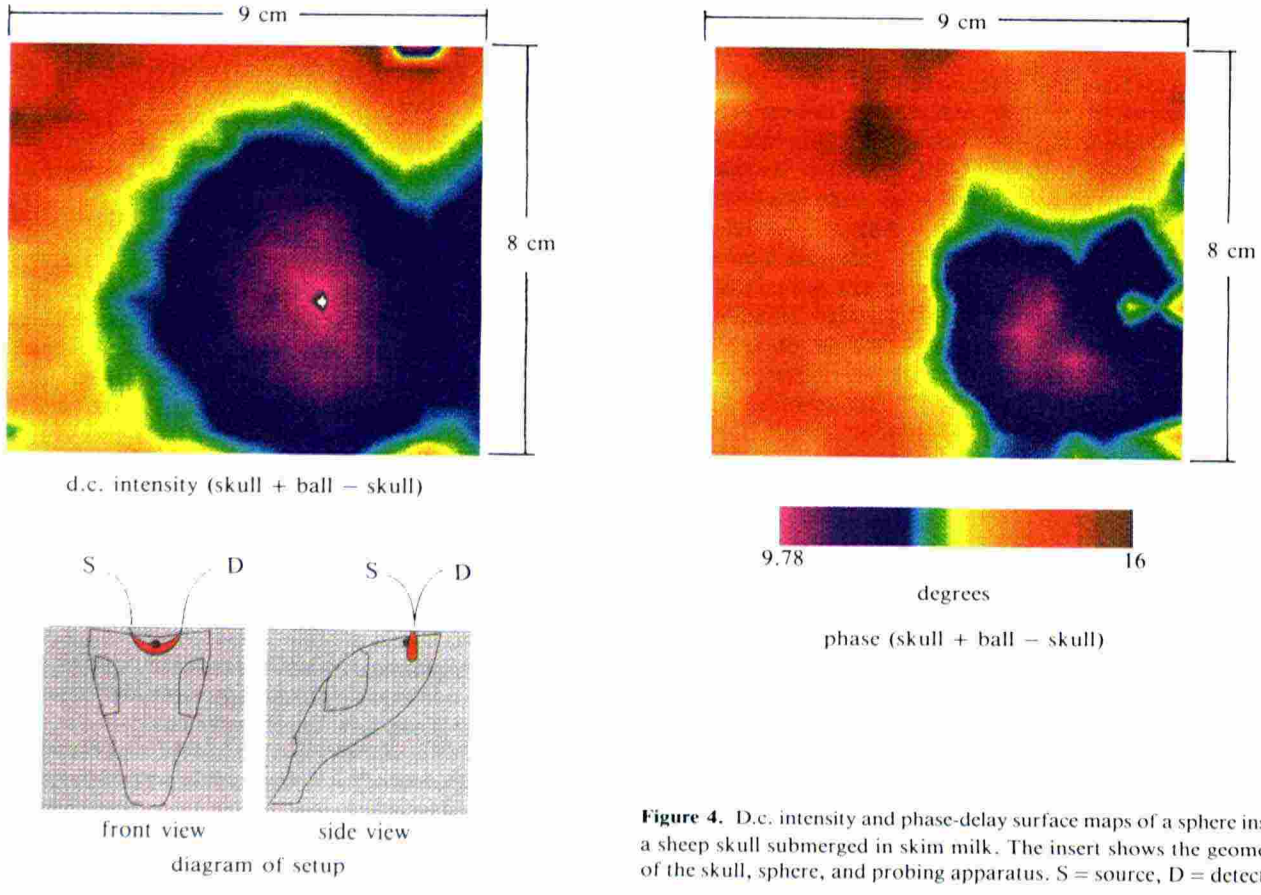

Figure 4. D.c. intensity and phase-delay surface maps of a sphere inside a sheep skull submerged in skim milk. The insert shows the geometry of the skull, sphere, and probing apparatus. S = source, D = detector.

Methods

The apparatus was similar to that described in Experiment 2. However, the absorbing sphere was inserted inside the cavity of a sheep skull submerged in skim milk. The effect of the skull was corrected for by subtracting a surface image obtained *without* the sphere in the skull from an image obtained *with* the sphere in the skull.

Results

The difference image is reported in Figure 4. Notwithstanding the distortion due to the skull, the ball is clearly visible. It shows unequivocally that the presence of an absorbing sphere located inside a skull can be demonstrated from measurements made outside the skull. Note that the effects of the sphere vary between 2 and 0.5 times those of the skull depending on the type of measurements (intensity, phase, or modulation) used.

Discussion

Our absorbing phantom was meant to mimic the situation of a hematoma in the brain. Our experimental data confirm the theoretical prediction (Svaasand, Tromberg, Haskel, Tsong-Tseh, & Berns, 1993) that near-infrared radiation penetrates the skull to sample deep structures. Ideally, the technique can be used to dynamically reconstruct, in a three-dimensional fashion, both the concentration and the distribution of target substances (such as oxy- and deoxyhemoglobin) within a particular body structure. Preliminary data indicate that a single-trial estimate of the concentration of these substances in tissue can be obtained with an average error of less than 5%. We are presently working on developing algorithms for three-dimensional reconstruction and multidimensional array detectors.

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