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BREAST CANCER IMAGING BY MEANS OF OPTOACOUSTIC TECHNIQUE: INITIAL EXPERIENCE

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A clinical prototype of the laser optoacoustic imaging system (LOIS) for breast cancer detection with 32-element transducer array is described. The frequency band of transducer array provided 0.5-mm axial in-depth resolution. Cylindrical shape of the 10-cm long array enabled us to receive the lateral resolution of 1.0 mm in the vicinity of focal zone. The system sensitivity provided detection of a 2-mm absorbing sphere at the depth of 60mm. An automatic recognition of the optoacoustic signal detected from the irradiated surface was implemented in order to visualize the breast surface and improve the accuracy of tumor localization. Radial back-projection algorithm was used for image reconstruction. Optimal filtering of image was employed to reduce low and high frequency noise. Time necessary for data acquisition and image reconstruction was reduced to 32 sec. The system performance was evaluated initially by imaging of the small absorbing objects in breast tissue-like phantoms. Clinical ex-vivo studies of mastectomy specimens were performed and compared with X-ray radiography and ultrasound.

1. INTRODUCTION

Optoacoustic tomography (OAT) is based on the differences in optical properties between cancerous and normal tissues. The major difference in absorption coefficient results from higher blood content in tumors compared with normal tissues [1] which in turn is associated with increased vascularization (angiogenesis) in rapidly growing tumors. Since hemoglobin of blood is the major chromophore in biological tissues in the visible and near infrared spectral range malignant tumors have higher absorption coefficient than normal tissues. Recent clinical studies that employed optical imaging techniques demonstrated existence of optical contrast of 200-300% between normal and cancerous tissues in the breast [2,3]. Illumination of the absorbing tumor by a laser pulse at 1060 nm wavelength with short duration results in instantaneous heat deposition inside tumor volume. Subsequent thermal expansion produces acoustic waves that propagate from the absorber surface. A temporal profile of the acoustic pulse generated upon instant heating of a spherical tumor has an N-shaped form with triangle compression phase followed by the rarefaction phase. The duration of the optoacoustic pulse is defined by the time of sound propagation along the diameter of the sphere: $\tau_a = 2a/c_0$ (here a is the tumor radius, c_0 is the sound speed inside tumor). The

absorbing energy and thermodynamic properties of absorbing tissue define a peak pressure of the emitted pulse. Tumors with dimensions of 1-10-mm irradiated with laser pulses represent themselves as sources of acoustic waves with ultrasonic frequencies of ~1 MHz to ~100 kHz. Such ultrasonic waves can propagate in biological tissues with insignificant attenuation and provide the information on the dimension and position of tumor. The optoacoustic tomography utilizes acoustic signals induced by laser pulses in tumors and detected by acoustic transducer [4]. Application of a wide-band acoustic detection in OAT instead of detection of photons in optical computer tomography (OCT) helps to overcome the problem associated with strong light scattering in biological tissues and increase depth of monitoring and spatial resolution [5].

2. MATERIALS AND METHODS

2.1. Laser optoacoustic imaging system

A Nd:YAG laser operating at the wavelength of 1064 nm was used as a source of near-infrared pulses of 10-ns duration. An optical fiber was employed for the laser pulse delivery to the tissue surface. Breast phantoms and mastectomy specimens were placed on the surface of the 32-element acoustic array. Transducer array housing was fixed vertically in a specially designed holder, which provided a convenient access to the samples. The 32 identical preamplifiers were placed in the same housing in the vicinity of transducers. Each preamplifier had a 1 MOhm electrical input impedance and low output impedance of 50 Ohm. The voltage of electrical signals from preamplifiers were amplified and digitized with a PDA-12 data acquisition card with two input channels. A multiplexor sequentially connected thirty-two amplifier outputs with the two input channels of the data-card. Acquired data were stored in a computer for further processing.

A specially designed array of PVDF acoustic transducers was employed in LOIS. The array had 32 rectangular piezoelectric transducers of 1x12.5 mm dimensions and 3.85 mm distance between transducers. Piezoelectric polymer PVDF of 110-μm thickness was used for transducer fabrication. Low acoustic impedance and ability to operate in wide ultrasonic frequency band are the advantages of PVDF for detection of opto-acoustic profiles. The transducers were located on the arc surface of 60-mm radius. This geometry provided a high resolution in the vicinity of focal zone. Backing material was used for mechanical matching of transducer and damping of acoustic wave reverberations after detection. The measured mean sensitivity for transducer array was about 6 μV/Pa [6].

2.2. Signal processing and image reconstruction

Each signal detected by acoustic transducers in the array consists of the following three components: (1) a sharp peak produced at the very surface of the medium under investigation, (2) a low-frequency smooth-rise exponential slope produced by the attenuation of light intensity inside tissue, and (3) short N-shaped pulses generated by small absorbing tumors. We assumed here that the tumor has a spherical form of radius a. The delay time of N-shaped signal arrival depends on tumor location relative to transducer. Therefore position of the tumor and its dimensions can be determined from the temporal course of an optoacoustic signal. First of all one should eliminate completely low frequency component of the OA signal associated with homogeneous light attenuation inside the tissue, because it can significantly decrease the image contrast. This was achieved in LOIS with high-pass numeric filtering. The signal generated by laser pulses in the subsurface layer (very close to the surface) possesses maximum amplitude over the entire detected course. The position of absolute minimum in the signal was considered as the position of the irradiated tissue surface.

The computer generated numerical signal at the surface position determined for each transducer and stored these data in a separate file. All data samples were cut off the signal after arrival of the signal generated at the tissue surface. Integrated signals were used as input data for the image reconstruction code. The surface-marks generated by computer were used for the surface visualization. Combined image contained the surface and the tumors, provided information about tumor location relative to the irradiated surface. A radial back-projection algorithm was employed for the optoacoustic image reconstruction. We used signal integrals and projected them back onto the two-dimensional grid taking into account the directivity pattern of each transducer. The resulted image represents distribution of a product of thermo-acoustic efficiency, optical absorption and absorbed laser energy. The back-projected images were noisy and their contrast was insufficient for correct object recognition. Therefore additional procedure of the image filtration was used.

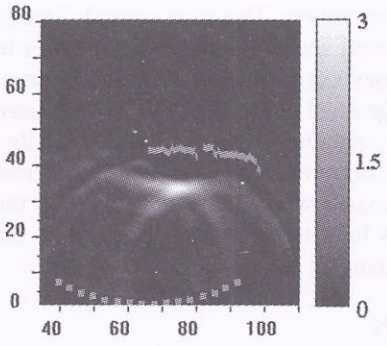

Figure 2. Optoacoustic image of the malignant tumor.

3. RESULTS AND DISCUSSION

3.1. Absorbing blood vessels in the gelatin phantom

A gelatin phantom with three blood vessels embedded inside it was used for the system testing. A phantom had a cylindrical shape with radius equaled to radius of the transducer array curvature. It enabled us to provide a perfect acoustics contact between transducer array and phantom surfaces. The effective light attenuation coefficient in the phantom of 1.2 cm^{-1} was similar to typical value for normal breast tissue *in vivo* at 1064 nm. Thin-walled plastic tubes filled with hemoglobin solution imitated small absorbing tumors. Their depths and corresponding light absorption coefficients were as follows: #1 (28 mm, 0.5 cm^{-1}); #2 (38 mm, 0.5 cm^{-1}); #3 (50 mm, 1.5 cm^{-1}). The gelatin phantom was placed on the transducer array surface, which was preliminary moistened in order to provide a sufficient acoustic coupling between phantom and the transducer. Laser light delivered with optical fiber illuminated the top surface of the phantom. The fiber was moved along the acoustic array axis with 6-mm intervals. Two-dimensional images of blood vessels arc presented in Fig.1. The relative position of vessels and their depths defined from image are in good agreement with their real location. Bright line on the top of the picture correspons to the phanton surface where ligth illumination took place. The optoacoustic contrast of the deepest vessel can be estimated as 200 %.

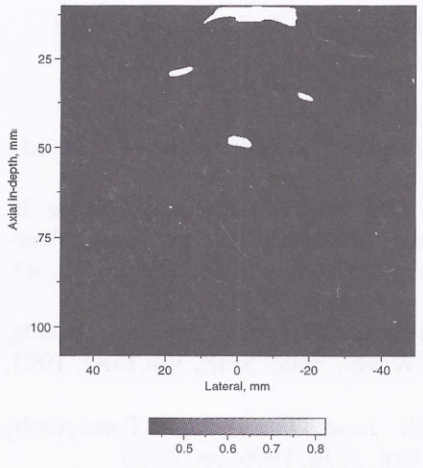

Figure 1. Optoacoustic images of blood vessels inside gel phantom

3.2. Breast mastectomy specimen

Breast specimens were obtained after radical mastectomy and examined within the first ten minutes after surgical excision. It provided specimens that underwent minimal alterations

of tissue optical properties, except some blood was drained form the specimens. The mastectomy specimens were measured to determine tumor geometry. Location of tumors was not known prior to opto-acoustic imaging procedure. However, tumors were sometimes palpable and biopsy incision was visible on the spared segment of skin. Optoacoustic image of breast with carcinoma is presented in Fig.2. Fifteen fiber positions with 4-mm interval were employed for data collection and subsequent image reconstruction. The scan passed directly over the tumor. The tumor core, horizontal tail and the small sprouts may be clearly seen in the opto-acoustic image (confirmed by subsequent pathology examination). The dimension of a tumor core can be estimated as 10x7 mm. Tumor was detected at the depth of 11 mm from the surface. Skin was removed from most part of the specimen, therefore the irradiated surface is depicted as a rough line. Contrast between the tumor and surrounding normal tissues in this image exceeds 350%. OA image was compared with ultrasound image of the same tumor obtained *in vivo*. The core of tumor and its long tail may also be seen in US image. However, small sprouts are not visible to limited acoustic contrast.

4. CONCLUSION

A clinical prototype of LOIS for early breast cancer detection with 32-element transducer array was developed and tested in phantoms and mastectomy specimens. Sensitivity of LOIS allows detection of 2-mm tumors at the depth of 6 cm. In depth resolution equals 0.4 mm, lateral resolution is 1-2 mm depending on position of tumor relative to the transducer array. This modification of the LOIS is the basis for a advanced system, which will be used for *in vivo* studies. *In vivo* optoacoustic imaging protocol is currently approved at UTMB.

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