Time of Flight THz Imaging of 3D Ex-Vivo Breast Cancer Tumor Tissues

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***Abstract*—This research represents experimental use of a pulsed terahertz time-domain imaging system to obtain time of flight (in-depth) reflection scans from three-dimensional ex-vivo breast cancer tumor tissue. Image processing and volumetric techniques are performed on these THz scans to analyze and enhance the tumor image and assess its boundaries.**

I. Introduction

Terahertz (THz) technology holds great potential for biomedical imaging. The non-ionizing nature of low power THz sources makes this application biologically safe [1]. This research is focused on THz imaging of three-dimensional (3D) breast cancer tissue, which is of particular interest due to the distinct electrical properties in cancer from the surrounding normal tissue at THz frequencies [2]-[5]. Terahertz imaging of relatively flat sections of breast cancer tissue has proved its effectiveness in distinguishing cancerous tissue from healthy tissue [2],[3]. Additionally, spectroscopy characterization has been performed to validate the differentiation between breast cancer and normal tissue at THz frequencies [2],[4]. However, the use of imaging for 3D tumor tissue blocks has yet to be adequately explored.

This work makes use of the Pulsed THz Imaging and Spectroscopy System at the University of Arkansas. Several samples of formalin-fixed paraffin-embedded (FFPE) breast cancer tissue adjacent to normal tissue in blocks were obtained from the National Disease Research Interchange (NDRI) and Northwest Arkansas (NWA) Pathology Associates for use in this work. The samples are originally embedded in paraffin blocks as bulk tissue. These blocks are then raster scanned in the x-y plane using 200 µm step size. Secondary reflections in the time-domain provide depth information throughout the block (known as the Z-scan). The depths of these reflections are calculated by relating the time between reflection peaks to the distance traveled through the tissue block. The samples are then physically sectioned into 20, 30, and 40 µm thick slices for correlation with histopathology images obtained through the block. These images indicate the regions of cancer, fibroglandular (fibro), and fatty tissues.

In order to enhance the THz Z-scan images, volumetric image processing techniques are utilized. These processes include unsharp masking, Gaussian smoothing, and the variance scheme. In addition, THz Z-scan imaging is also used on tissue phantoms of fibro, fatty and cancerous tissues to investigate THz interaction with materials that mimic freshly excised tumors. The phantoms are matched to the dielectric properties of fresh breast cancer tissue [6],[7].

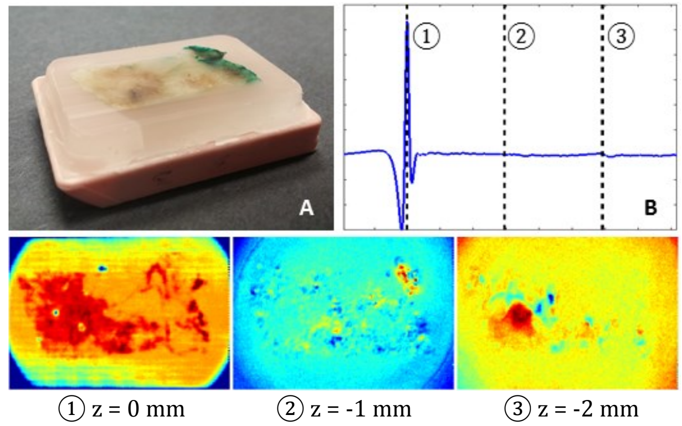

Fig. 1. THz Z-scan imaging of breast cancer tumor tissue embedded in paraffin. (A) Tissue block photograph. (B) Measured reflected time-domain signal at a single pixel, and time of flight cross section images obtained at ① z = 0 mm (surface of tissue block), ② z = -1 mm (inside the tissue block), and ③ z = -2 mm (inside the block near the bottom of the tumor tissue).

II. Results

Fig. 1 shows imaging results obtained from the time-domain scan of a breast cancer tumor with adjacent healthy tissue embedded in a paraffin block. The physical block in Fig. 1A is scanned to obtain a reflected signal at each point, as shown for one pixel in Fig. 1B. At any given time in the reflected signal, it is possible to obtain a cross-section image at the depth associated with that time. This technique is known as time of flight. Three time locations are selected as shown by the dotted lines in Fig. 1B. The images denoted by ①, ②, ③ correspond to the depth locations associated with the selected times, z = 0, -1, and -2 mm, respectively. The image ① represents the surface reflection of the block with the highest reflection (red color) region indicating the cancer tissue. The image ② at z = -1 mm shows that there are few notable reflections within the tumor. Finally, the image ③ at z = -2 mm shows reflection from the other side of the tumor tissue.

The image processing techniques can be employed to further improve the images taken from the Z-scan. Some of the processing in use at present work includes row alignment, unsharp masking, variance method, and histogram equalization. Row alignment is an automated process used to line up the even and odd rows in the scan data due to an offset of one or two pixels introduced by the raster scanning motors of the THz system. Local error assessment is used to determine the best fit alignment of each row and shifts the data accordingly. Unsharp masking is a technique that creates a blurred dataset from the original dataset and subtracts it, enhancing any small features in the signal. The blurred dataset for this task is obtained by taking a local average around each point in the original dataset. The strength of the blurring is also adjusted to obtain the best results. The variance method is also used to emphasize small features, though it does so by calculating the local standard deviation of each point in the scan and adjusting it such that the variance is roughly the same across the entire scan. Fig. 2 shows the results of some of the image enhancement techniques performed on a THz scan of cancer tumor with adjacent healthy tissue. It can be seen that moving from the original THz image in Fig. 2A to the processed image using unsharp masking (Fig. 2B) and variance method (Fig. 2C) shows an improvement in the clarity between regions in tissue with both methods.

(A) (B) (C)

Fig. 2: Results of image enhancement of x-y cross section of FFPE cancer tissue with adjacent fibroglandular tissue. (A) Original THz image, (B) with unsharp masking, and (C) with variance method.

Another method of identifying the location of interfaces within the sample is to take a cross section of the Z-scan along the x-z or y-z axes. From these cross sections it is possible to view several reflected signals in a line to determine where any additional reflections occur within the measured signals. This can be seen in Fig. 3 for the same data obtained from the fixed tissue in the paraffin in Fig. 1. This data is compressed in the z-axis using averaging in order to provide reasonable dimensions for the images. Additionally, uniform scaling is used to give reflections at any depth in the block the same intensity as the primary reflection at the surface of the block. This is done by adjusting the values of each x-y cross-section to have the same scale. Finally, unsharp masking is used to refine the scan features. This technique is chosen over the variance method due to the unsharp masking producing less noise through the depth of the scan. In the resulting dataset, the x-z plane and the y-z plane taken through the middle of the sample reveal the various reflections seen throughout the block. In particular, strong reflections are seen near the bottom of the z-scan, which denote the interface between the tumor and the paraffin. From these results it is possible to determine the 3D boundaries of the embedded tumor.

In order to assess the ability of the Z-scan to provide depth and volume information in fresh tissue, solid phantom materials have been prepared with water, olive oil, surfactant, and TX151 solidifying powder [7]. The use of the prepared phantom allows for more controlled thicknesses of tissue that could then be compared to the estimated depths.

III. Summary

Time domain THz imaging has been shown to be effective in 3D imaging of fixed and phantom breast tumors and is suitable to time-of-flight calculations for volume analysis. Image enhancement has been performed on both fixed tissue and breast tumor phantoms.

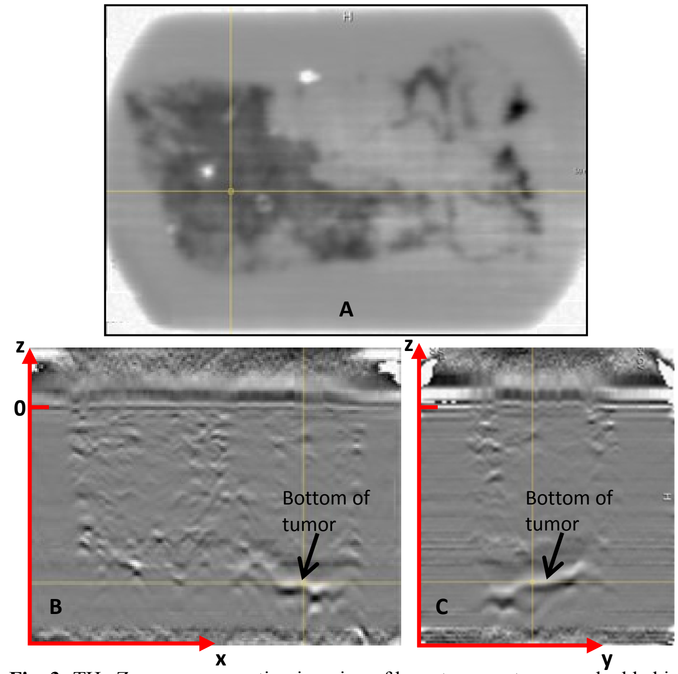

Fig. 3: THz Z-scan cross-section imaging of breast cancer tumor embedded in paraffin after image enhancement using unsharp mask and uniform scaling methods. (A) x-y cross section taken from surface reflection (z = 0), (B) x-z cross section, (C) y-z cross section.

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