A primary research of the relationship between breast tissues impedance spectroscopy and Electrical Impedance Scanning

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***Abstract*—*Objective* To study the electric impedance properties of healthy and malignant breast tissue and their relationship with the image of Electrical impedance scanning (EIS).** *Method* **The impedance character of 40 malignant tumors, 34 benign tumors and some normal breast tissues from 69 patients undergoing breast surgery who had been examined by EIS *in vivo* measurement and mammography screening were analyzed, with a series of frequencies set between 100Hz-100kHz in the *ex vivo* spectroscopy measurement.** *Result* **Of the 39 patients with 40 malignant tumors, 24 showed bright spots, 11 showed dark area in EIS and 5 showed no specific image. Of all the 30 patients with 34 benign tumors were almost no specific abnormality shown in EIS results. Primary *ex vivo* spectroscopy experiments show that the resistivity of various breast tissue take the following pattern: adipose tissue>cancerous tissue>mammary gland and benign tumor tissue.** *Conclusion* **There are significant difference in the electrical impedance properties between cancerous tissue and healthy tissue. The impedivity of benign tumor is lower, and is at the same level with that of the mammary glandular tissue. The distinct growth pattern of breast lesions determined the different electrical impedance characteristic in EIS results.**

Keywords- ***breast cancer; electrical impedance scanning;spectroscopy measurement***

I. INTRODUCTION

In recent decades, electric and dielectric measurements have been carried out in breast tissue under a range of experimental conditions including *in-vivo* or *ex-vivo* measurements and using various measurement techniques [1-9]. The same conclusion was that a statistically significant difference in the electrical impedance property exists between malignant tissue and healthy tissue.

Based upon these findings, a new imaging modality for measuring and visualizing electrical-impedance changes within the breast has been developed. Electrical impedance scanning (EIS) was performed with the TransScan TS 2000 electrical impedance scanner. TransScan TS 2000 has been tested at various breast centers all over the world [10-18], but up till now there were many unanswered questions that require further investigations.

We've been using EIS as a routine examination for women and found a majority of breast cancers showed high conductivity (bright white spots) in EIS image. Some showed low conductivity (dark area) and the displays of benign tumors were almost homogeneous gray. We seldom got the report about malignant tumors that showed the low conductivity in EIS results and the reason why benign tumors were rarely detected by EIS had not been demonstrated clearly. In order to explain these phenomena about different characteristic of EIS image, and to further investigate the possibility of distinguishing tumor by EIS, a clinical EIS and a parallel electrical impedance measurement of surgically removed tissue for measuring and comparing the impedance spectra of tumor tissue and healthy tissue were done.

II. MATERIAL AND METHODS

A. Electrical Impedance Scanning (EIS)

Our research group developed an EIS device for breast examination in 2003 [19-20] (see Fig.1). It is mainly consisted of a reference electrode and a scan probe, in which there were a rectangular array of 8 × 8 electrodes. The driving voltage is from 0.1V to 2.5V and the measurement frequency range is from 50 Hz to 20 kHz. A set of algorithms translates the quantitative data sets to yield gray-scale images, where the healthy breast tissue shows a homogeneous distribution of the applied current, with uniform conductivity and capacitance values. A focal increase of electrical conductivity or capacitance caused by cancerous tissue distorts the electrical field within the breast and appears as a focal brightness (a white spot) on a gray scale map of the monitor. Each spot representing high conductivity or capacitance that was not caused by skin surface lesions or artifacts (poor contact between probe and skin, or air bubbles within the contact gel and ribs et al) was interpreted as positive EIS finding. The absence of a spot within the region of the breast corresponding to the mammographic or clinical finding or both was interpreted as negative EIS finding.

Figure 1. EIS instrument

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EIS has two different examination modes: the scan mode and the targeted mode. The scan mode examined the entire breast and the targeted mode scanned a suspicious region of the breast. The assessment of all examinations in the scan mode was performed at the default frequency of 200 Hz. In the targeted mode, multiple driving frequencies could be switched, and controlled by the software. During the multi-frequency examination, the operator can easily obtain a serial measurement about one interest sector with varying driving frequencies, while the other conditions remain approximately unchanged.

B. Ex vivo Measurements of Tissue Samples

We obtained 40 malignant tumors, 34 benign tumors and some normal breast tissue *ex vivo* from 69 patients undergoing breast surgery. All the cases were from the first affiliated teaching hospital of the Fourth Military Medical University.

We used frequency response analyzer 1255B (0.1Hz to 1MHz), impedance measurement software (3.1.0 version) and its impedance/gain phase graphing and analysis software 1294 (2.1 version), all developed by Solartron Mobrey Ltd. Four silver electrodes (Φ 1mm diameter, 4 mm apart) were arranged in a row in the measure tank (Fig.2) and used for impedance measurement. Electromagnetic shield and EIS system were also made by our research group.

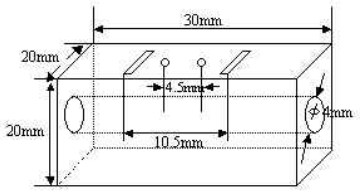


Figure 2. Measurement tank.

C. Methods

For breast imaging, mammography is practical as measured by its achievable performance and is established standards. In this research, mammograms were done after the clinical breast examination (CBE) results of patients were palpable lesion present. Then patients who were suspected breast neoplasm (diagnosed by mammography) were selected to enroll this research. EIS was done in the outpatient department and *in vivo* multi-frequency scanning was done to create a whole EIS image in the tumor sectors. After this, the patients were subjected to surgery during which biopsies were obtained and *ex vivo* spectroscopy measurement was done immediately in the operation room. The impedance spectroscopy results of the surgically removed breast components including glandular tissue, adipose tissue, nipple and skin were measured. The tissue was trimmed into a cylinder and wiped away blood and body fluid and then put into the measurement tank (Fig. 2). The four silver needle electrodes were connected to the instrument through a 4 way shielded wire and the four-electrode technique was used. The whole system was kept in the electromagnetic shield and the operation room with temperature fixed to 22±1 ℃. All the measurements were finished within 30 min after removal of the specific tissue. Different frequency check point was set between 100Hz－100kHz with 10 measurements per decade of frequency. Each spectrum consisted of 30 frequency points. All the tissues that had been measured were at last fixed by 10% neutral formalin and embedded in paraffin, sectioned to 4μm thick and stained by hematoxylin-eosin (HE). Final diagnoses of the tissues were based on microscopic examination by experienced technicians in the department of pathology in this hospital.

III. RESULTS

During the modified radical mastectomy or lumpectomy, we got the different breast tissue samples to receive the spectroscopy measurement and the diagnosis was based on pathological evidences. Of the 39 patients with 40 malignant tumors, 24 showed bright spots, 11 showed dark area in EIS and 5 showed no specific image. Of all the 30 patients with 34 benign tumors, there were almost no specific abnormalities shown in EIS results. The age of the patients ranged from 18 to 74 years old.

Primary analysis based on the spectroscopy measurement results of 40 independent measurements of cancerous tissues and 34 benign tumor tissues show that the resistivity of various tissues take the following pattern: adipose tissue 2086±345.8 Ω cm (n=41)>cancerous tissue 400 ± 43.6 Ω cm (n=40)>mammary gland 255±32.1 Ω cm (n=49) and 231±15.9 Ω cm (n=22) for fibroadenoma. The results we got from the complex plane show that there were significant differences in the impedivity values between cancerous tissue and healthy tissue, especially adipose tissue where the electrical impedance could be as high as 4 to 6 times as compared with healthy tissue. Fig. 3 shows the typical spectra of adipose tissue, fibroadenoma, mammary gland and carcinoma. The bio-impedance of most tissue obeys the Cole-Cole circular arc law. It's analogical in the change trend of the impedivity curves of different breast tissue, but their distribution location in the complex plane is not the same. To clearly illustrate the change trend of different breast tissue, we didn't plot them in the same

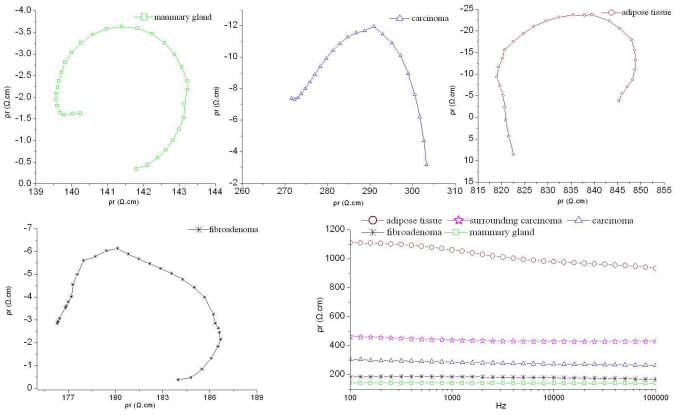
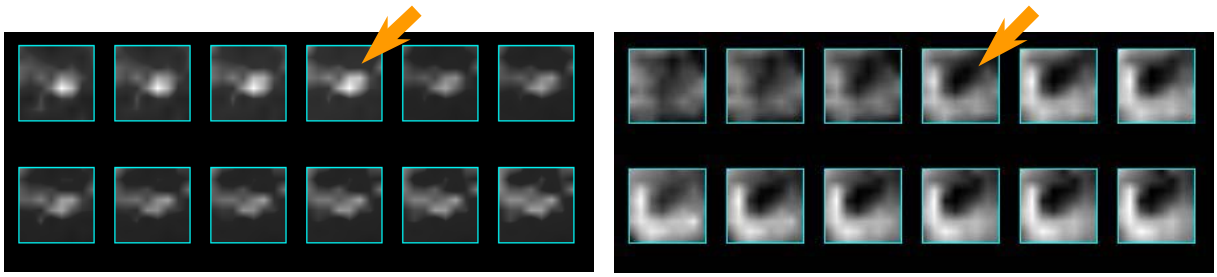


Figure 3. Impedance spectroscopy measurement for breast tissues.

complex plane. Along with drive frequency rising, the data of the real axis are decreasing and the absolute values of the imaginary axis are rising first and falling later. The frequency where the magnitude of the imaginary component passes by a maximum is defined as 'top frequency'. This parameter may help us to distinguish between different breast tissues in the further study.



4-a 4-b

Figure 4. Mammary cancerous image in EIS.

The basic goal of EIS is to use the healthy tissue as the reference and to pick up the difference of electricity signal between breast tumor and healthy tissue. When the difference between them exceeds a certain degree, the images of EIS will show higher or lower signals. In the result of 40 malignant tumors, we got some bright or dim spots on the EIS images. The spots in Fig.4 (4-a) correspond to focal increase of conductivity and capacitance caused by the images shown previously signalized as mammography suspicious zones and Fig.4 (4-b) showed lower conductivity characteristic of malignant tissues under the EIS multi-frequency scanning in targeted mode. The reason for this phenomenon we primarily got by combining with their impedance spectroscopy measurement in discussion. This EIS images (Fig. 4) in the targeted mode got from two patients (histological diagnosis: invasive ductal carcinoma) with multiplicity of signals for conductance in tumor sector, and simultaneous presence of capacitance and conductance signals. Upper sectors show conductivity images and lower sectors capacitance images.

Although the conductivity difference between malignant tissue and normal breast tissue (the values of mammary tissue around the tumors) is evident ($P<0.01$), the value is not significantly different between benign tumor, especially between fibroadenoma and mammary gland of the breast ($P>0.05$). Statistical analyses were conducted by means of Kruskal-Wallis test and analysis of variance, and P values less than 0.05 were considered significant. In other words, admittivity of benign tumor is higher than of malignant tumor.

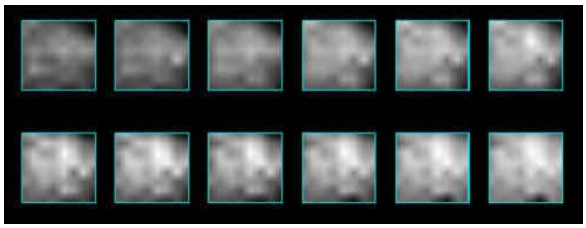


Figure 5. Fibroadenoma image in EIS.

However, during the EIS examination, the results of 34 benign tumors rarely display fine conductivity characteristic (bright white spot) and the images always showed gray which were similar to normal tissue. Fig. 5 showed the fibroadenoma image from one patient under the multi-frequency scanning in the EIS targeted mode and the area displayed was relatively homogeneously gray, because there was probably no enhanced current signals measured by the nearest sensing electrodes. Upper sectors showed conductivity images and lower sectors capacitance images. The present phenomenon led us to continue the study on how to distinguish benign tumor from malignant tumor with EIS.

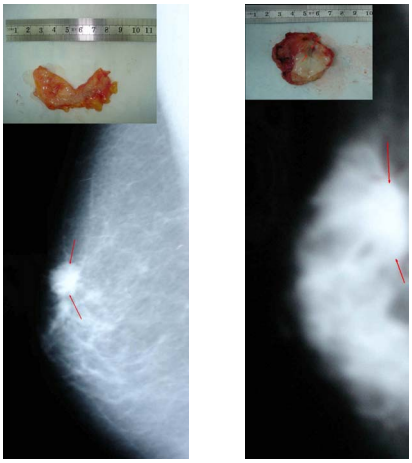
IV. DISCUSSION

We learn from the pathology that the growth of breast cancer is an invasive pattern that could invade any surrounding tissue. If the mainly surrounded tissue were the gland, cancer cell would make an invasion upon it and the same as adipose tissue. In despite of the fact that cancer cell could make an invasion upon any surrounding tissue, we found from the spectroscopy measurement of the breast that there are significant admittivity difference between them. Whenever this difference is high or low in conductivity, the resulting image of EIS would show bright or dim spots. This could probably explain some phenomenon we encounter during our clinical EIS measurement.

Looking in greater detail at the breast cancer of Fig. 4-a for example, which is now shown in greater detail in Fig. 6-a. This patient received a mastectomy and breast tissue was made available to us. We combined the mammogram with surgery specimen of the malignant tumor and surrounding tissue. Mammogram (MMG) result (Fig. 6-a): there was a small tumor in the upper lateral quadrant of the right breast, round in shape, 1.0×1.2cm. The anterior boundary of the tumor was clear and the posterior boundary was blurry. The tumor tissue that was solid, section gray, boundary blurry and invasive in surrounding tissue that was adipose tissue and was proved to be infiltrating ductal carcinoma pathologically. The impedivity of the tumor and the surrounding adipose tissue were measured by impedance spectroscopy. From the tumor tissue and MMG image (Fig. 6-a), we could learn that this was primarily fatty breast in which mammary gland was degenerative. The invaded tissue was mainly adipose tissue.

On the other hand, based on the breast cancer of Fig. 4 (4-b), we made the same comparison between MMG result and specimen of the malignant tissue and the surrounding tissue. MMG result (Fig. 6-b): there was a 1.5×2.0 cm asteroid tumor in the upper medial quadrant of the right breast. During the breast surgery, we got the specimen that was solid, section gray, boundary blurry and invasive in mammary gland. Pathological diagnosis proved to be infiltrating ductal carcinoma. The resistivity of tumor and surrounding glandular tissue were obtained from spectroscopy measurement. From the specimen and MMG image (Fig. 6-b), we concluded that this was dense breast and the growth of tumor was invasive pattern. The invaded tissue was mainly mammary gland.

These are in good accord with what we found in EIS where cancerous lesions (high conductivity/low impedance) surrounded by adipose tissue (low conductivity/high impedance) showed as bright regions (Fig. 4-a). When the cancerous lesion was surrounded by tissue that was more



6-a 6-b

Figure 6. Difference invasive pattern of malignant tumors.

conductive than itself, a region dominated by glandular tissue for example, the lesion appeared as a dark spot on EIS (Fig. 4-b).

In our preliminary findings, the conductivity of benign tumors, especially fibroadenoma was higher than that of malignant tumor and benign tumor usually did not show up clearly on EIS images. These findings were against what we had assumed formerly. There could be some factors that may explain these problems. One reason is that fibroadenoma is mainly composed of fibrous tissues and mammary gland, both have a high admittivity. So, fibroadenoma has a better conductivity too. Secondly, benign tumor is usually confined within its outer membrane and seldom invades into adipose tissue that has high resistance. The outer membrane of the tumor whose electrical resistance is greater and thus might neutralize the high conductivity of its content located within. On the other hand, the growth of benign tumor is in an expansible pattern and the boundary is clear. Taken Fig. 7 for example, the MMG result showed that: there was a 3.0×4.0 cm rounded lump in the top left breast which had a clear boundary. During the breast surgery, we got the tumor that bore a whole membrane, clear boundary and offwhite section. Pathological diagnosis was fibroadenoma. The resistivity of tumor was obtained by impedance spectroscopy. From the MMG image, we could see that this was a dense breast and the tumor-surrounding tissue was mammary gland. With the glandular tissue around, whose resistance is relatively comparable with the tumor itself, contrast is usually not significant. But, malignant tumor usually invades into adipose tissue that contrasts greatly with the tumor. So, in theory, EIS could distinguish between benign tumor and malignant tumor. However, there are still some technical problems that need to be solved before this could be achieved, such as: contact resistance varied greatly and the influence of tumor size and depth on accuracy in EIS, *et al*.

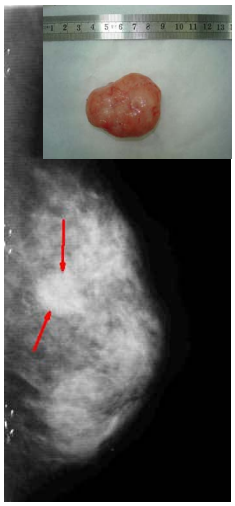


Figure 7. Living pattern of fibroadenoma.

V. CONCLUSION

Electrical impedance scanning is a non-invasive, radiation-free technique that maps the local electrical impedance properties of breast tissue to differentiate between healthy and malignant tissue. Primary spectroscopy experiments show that there are significant difference in the electrical impedance properties between cancerous tissue and healthy tissue and the impedivity of benign tumor is lower which is at the same level with that of the mammary gland tissue.

So, if malignant tumors invaded different surrounding tissue (adipose tissue or mammary gland) and the conductivity between them was dissimilar clearly, the results of EIS images would show up high or low (white or dark) electrical impedance characteristic. On the other hand, the difference of admittivity between benign tumors and their surrounding tissue was small, and this was mainly determined by the growth pattern of benign tumor and so they hardly displayed any obvious characteristic in EIS images.

Since measurements in breast disease (*ex vivo* and *in vivo*) are difficult and various, we would keep on doing a series of researches about it in the future.

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