Monitoring tumor response during chemotherapy treatment with Microwave Imaging

Aleksandar Janjić¹, Tuba Yılmaz¹, Mehmet Çayören¹, Ibrahim Akduman¹ and Lorenzo Crocco²
¹Istanbul Technical University, Electrical and Electronics Engineering Faculty, 34469 Maslak, Istanbul, Turkey
²Institute for Electromagnetic Sensing of the Environment, National Research Council of Italy, CNR-IREA, Napoli, Italy
E-mail: janjic19@itu.edu.tr, tuba.yilmaz@itu.edu.tr, cayoren@itu.edu.tr, akduman@itu.edu.tr, crocco.l@rea.cnr.it

Abstract—Chemotherapy treatment is a commonly used approach for treatment of localized malignant breast tumors. Ensuring accurate and reliable monitoring of the malignant tumor response to therapy can lead to the better follow-up care; thus, it would aid to increase the patient survival rate. In this paper, we introduce a microwave imaging system that can be used for breast cancer diagnostics and monitoring. The system is modeled in CST Microwave Studio and homogeneous breast model was used in order to assess its performance. Additionally, we propose a qualitative inverse scattering approach based on factorization method which allows us to monitor disease’s evolution during and after the treatment. Results reported present preliminary assessment of proposed imaging approach and serve as a guideline for future work considerations.

Index Terms—Treatment monitoring, microwave imaging, CST, breast cancer

I. INTRODUCTION

Presurgical chemotherapy has widely been used for treatment of breast cancer giving the possibility of tumor shrinkage which can lead to breast conservation and operable cancer cases. Therefore, there is a great need for development of harmless and more reliable imaging techniques that will give insight into tumor therapy response. Nowadays, conventional X-ray mammography is commonly used in order to detect breast tissue abnormalities. Due to X-ray mammography limitations, such as false-positive representations which can lead to unnecessary interventions or low sensitivity, in the cases of highly dense breast [1,2], other screening approaches had been considered in order to improve follow-up care.

Microwave imaging (MWI) represents a promising screening alternative due to the reported dielectric contrast between malignant breast tumors and normal breast tissue [3–5]. Up until now, a significant number of studies on implementation of microwave technology concept in medical screening has been done [6–10]. Within the framework of Electromagnetic Imaging for a Novel Generation of Medical Devices (EMERALD) ongoing project [11], our aim is to develop a new MWI device that will target the follow-up of breast cancer chemotherapy, in order to monitor the progression of the malignant tumor. The idea of using MWI for monitoring chemotherapy treatment response was previously introduced by [12]. But, unlike the approach proposed in [12], where tomographic methodology was considered in order to follow-up malignant tumor progression, more specifically where the tumor progression was followed by the change in electrical properties of the tumor itself, we rather consider the tumor geometry in order to follow-up the chemotherapy treatment response.

In this paper, we present the initial studies concerned with this project and in particular we assess the capabilities of a qualitative imaging method to accurately monitor the progression of the treatment. The aim is to assess the tumor therapy response by observing the change in size of the tumor tissue. To this end, the qualitative imaging result is post-processed with an edge preserving filter which allows to quantitatively appreciate the size of the treated region. Such a concept is assessed with a numerical analysis concerned with a piece-wise homogeneous breast model which includes the most important breast tissue (e.g. skin, fat and glandular).

II. IMAGE RECONSTRUCTION ALGORITHM

Developing an imaging algorithm that will be specifically meant for chemotherapy treatment monitoring represents important step towards MWI medical screening implementation. In order for the algorithm to be implemented, it needs to be able to cope with real life limitations (e.g. patient specific breast tissue structure, arbitrary breast shape, breast size).

To cope with the underlying non-linear and ill-posed inverse problem, more precisely to detect the shape and location of the tumor from the measured field it scatters, we have chosen as a starting point the factorization method (FM) [13], which is a qualitative inversion method by which image formation is carried out by the solution of auxiliary linear inverse problem. As such, the non-linearity of the problem is overcome (actually, this is traded by the impossibility of achieving information on the images tissue EM properties, but this is acceptable in the present problem, wherein the goal is monitoring not diagnosis and therefore the scenario is to some extent known). Implementation of FM is quite straightforward and requires that the domain of interest $\mathcal{D}$ is sampled into an arbitrary grid of points in which, for every point $\mathbf{r}_p$, the following linear inverse problem has to be solved:

$$\mathbf{F}_m[h(\theta, \mathbf{r}_p)] \psi_{\omega} = (\mathbf{r}_p, \varphi)$$

where $\psi_{\omega}$ stands for the Green’s function of the background medium in the sampling point evaluated at receivers.

$\mathcal{F}$ stands for the Green's function of the background medium in the sampling point evaluated at receivers.
Since $T_m$ is compact operator, eq (1) is ill-posed. Thus, in order to avoid instabilities, it has to be regularized. By exploiting singular value decomposition (SVD) [14] of $T_m$ as in form of $[\mu_n \sqrt{\xi_n}]$ the solution of eq (1) can be given as:

$$h(\theta, r_p) = \sum_{n=0}^{\infty} \frac{1}{\sqrt{\xi_n}} < \psi_n(t_p, \varphi), \mu_n(\varphi) > \mu_n(\theta). \quad (2)$$

Additionally, by exploiting Tikhonov regularization [14] a stable solution is explicitly achieved in the form:

$$h(\theta, r_p) = \sum_{n=0}^{\infty} \frac{\sqrt{\xi_n}}{\xi_n + \alpha} < \psi_n(t_p, \varphi), \mu_n(\varphi) > \mu_n(\theta) \quad (3)$$

where $\alpha$ denotes for Tikhonov regularization parameter.

The image of the target is given by an indicator function obtained by computing the L2 norm of the solution (3) over the grid.

One of the issues of qualitative methods such as FM is that the resulting image offers an estimate of the target’s shape, wherein however there is an uncertainty on the actual size of the target due to the not step-like transition of the indicator function. In order to cope with such boundary blurring, our implementation of FM is equipped with a post processing stage, exploiting an edge preserving filter. In particular, we used the guided filter approach [15]. Guided filter was chosen because it has good edge-preserving smoothing properties as well as it does not suffer from the gradient reversal artifacts [15], meaning it will not introduce false boundaries in the filtered image.

More in detail, the filtering process includes a guided image $I$, a filtering image $p$, and an output image $q$. Both $I$ and $p$ are given beforehand according to the application, and they can be identical. The filtering output at a pixel $i$ is expressed as a weighted average:

$$q_i = \sum_j W_{ij}(I)p_j. \quad (4)$$

where $i$ and $j$ are pixel indexes, and $W_{ij}$ is a filter kernel which is a function of $I$ and is independent of $p$. The filter itself is linear with respect to $p$ [15].

Filter kernel $W_{ij}$ can be represented in the form:

$$W_{ij}(I) = \frac{1}{|w|^2} \sum_{k \in |l_j| \neq w_k} \left(1 + \frac{(l_1 - \mu_k)(l_j - \mu_k)}{\sigma^2_k + \epsilon}\right). \quad (5)$$

where $\sigma^2_k$ represent variance, $|w|$ number of pixels in window $w_k$ centered at the pixel $k$ and $\epsilon$ stands for regularization parameter.

In our case, creating guided filter input $I$ requires two multi-static scattered field measurements corresponding to two different states of the breast – the pre-therapy breast and post-therapy breast. Similarly, filtering input $p$ requires additional multi-static scattered field measurements corresponding to also two different states of breast – in this case healthy breast and post-therapy breast

### III. PERFORMANCE ASSESSMENT

In this section, we provide some preliminary results considering approach proposed in section II. The piecewise homogeneous breast model adopted in this study, together with the antenna array adopted to probe it are shown in Figure 2. Breast model is composed of three tissue types: skin tissue, breast fat tissue and glandular tissue. Breast tumor was mimicked by spherical object buried inside breast glandular tissue. Dipole antennas were used for imaging purposes. MWI setup was modeled inside CST Microwave Studio (CST MWS). Antennas, as well as breast model, were immersed in properly defined matching medium in order to increase penetration depth of electromagnetic radiation.

![Figure 2. MWI setup consisting of dipole antenna array and homogeneous breast model immersed in matching medium.](image)

![Figure 3. Median plane section of the breast model indicating tumor location inside glandular tissue layer.](image)
Necessary data is acquired for two cases. More specifically, for the case in which the target size is largest, implicating the pre-therapy case, and for the case in which the size of the target is reduced due to the therapy effectiveness. Breast tissue dielectric properties were chosen according to the values reported by [16], while a spherical shape objects dielectric properties were defined as $\varepsilon = 56.0459$ and $\sigma = 1.48043$ S/m. Both, breast tissue and malignant tumor dielectric properties were chosen according to the characteristic frequency of 2 GHz. Matching medium dielectric properties were chosen as $\varepsilon = 4$ and $\sigma = 0$ S/m. Diameter size of the pre-therapy and post-therapy target cases are 30 mm and 10 mm respectively. Synthetic data are corrupted by white Gaussian noise with the SNR of 20 dB. Additionally, in order to provide quantitative information about similarity between the filtered results and exact form of the target, well-known Jaccard index [17] indicator is presented. Indicator is given by:

$$J_{acc}(\%) = 100 \times \frac{N_{cp}}{N_{up}}$$

where $N_{cp}$ stands for number of points for which $W_{b,exact}(r_p) = W_b(r_p) = 1$ and $N_{up}$ stands for number of points in which $W_{b,exact}(r_p) = 1$ or $W_b(r_p) = 1$. $W_{b,exact}(r_p)$ and $W_b(r_p)$ stands for exact binary indicator and binary indicator respectively.

For each case (pre-therapy and post-therapy) reconstruction, an edge-preserving filter is applied in order to enhance target boundaries. In addition to edge preserving, edge filtering is applied in order to qualitatively determine target size reduction. For this feature to be achieved, two different data types which are representing guided (I) and filtering input (p) of the filter (see section II) should be created. In order to determine the exact size of shrank target, input image p is filtered in the way that filtering process is guided by binarized guided image I. By applying this additional step, the exact size (post-therapy case) of the target of interest is achieved. The process and a sample output have been presented in Figure 4. From the Figure 4, it can be seen that with proposed approach we are able to obtain accurate results for simplified homogeneous breast model. Conformation that the exact size is achieved is given by a post-treatment target size a-priori information.

![Guided filtering process](image)

**Figure 4.** Illustration of the guided filtering process in the case of qualitative monitoring of target size variation.

In this paper, as a part of preliminary research activities within EMERALD project, a qualitative inverse scattering approach for monitoring the progression of chemotherapy has been proposed. The adopted imaging approach is reliable and capable of providing real-time images, and its intrinsic limitation in deriving the exact size of the target (i.e. the shrinking tumor) is dealt with a post processing stage exploiting the guided filter technique as an edge-preserving tool. The results show that this procedure allows to enhance the accuracy in estimating the edges of reconstructed object as well as to track size variation of the object itself.

As an example of this study, a reconstruction results are shown, from which it is possible to appraise the importance of the post-processing step. It is worth mentioning that in order to confirm the validity of edge-preserving feature, which is providing qualitative information considering target size variation, an a-priori information about the target pretreatment and post-treatment size should be available.

In order to further assess and improve the proposed approach, further research activities are ongoing, aimed at enhancing algorithm performance by embedding into it an a-priori information from other diagnostic modalities (e.g. MRI).
ACKNOWLEDGMENT

This work was supported by the EMERALD project funded from the European Union’s Horizon 2020 research and innovation program under the Marie Skłodowska-Curie grant agreement No. 764479.

REFERENCES

1. Lashof, J. C., Henderson, C., Allred, D. C. & Baum, J. K. Mammography & Beyond: Developing Technologies for the Early Detection of Breast Cancer. 1–8 (2001).
2. Huynh, P. T., Jarolimek, A. M. & Daye, S. The False-negative Mammogram. Radiographics 18, 1137–1154 (1998).
3. Surowiec, A. J., Stuchly, S. S., Barr, J. R. & Swarup, A. Dielectric Properties of Breast Carcinoma and the Surrounding Tissues. IEEE Trans. Biomed. Eng. 35, 257–263 (1988).
4. Lazebnik, M. et al. A large-scale study of the ultrawideband microwave dielectric properties of normal, benign and malignant breast tissues obtained from cancer surgeries. Phys. Med. Biol. 52, 6093–6115 (2007).
5. Lazebnik, M. et al. A large-scale study of the ultrawideband microwave dielectric properties of normal breast tissue obtained from reduction surgeries. Phys. Med. Biol. 52, (2007).
6. Winters, D. W., Shea, J. D., Kosmas, P., Van Veen, B. D. & Hagness, S. C. Three-dimensional microwave breast imaging: Dispersive dielectric properties estimation using patient-specific basis functions. IEEE Trans. Med. Imaging 28, 969–981 (2009).
7. Winters, D. W., Van Veen, B. D. & Hagness, S. C. A sparsity regularization approach to the electromagnetic inverse scattering problem. IEEE Trans. Antennas Propag. 58, 145–154 (2010).
8. Zhang, Z. Q. et al. Microwave breast imaging: 3-D forward scattering simulation. IEEE Trans. Biomed. Eng. 50, 1180–1189 (2003).
9. Meaney, P. M., Fanning, M. W., Li, D., Poplack, S. P. & Paulsen, K. D. A clinical prototype for active microwave imaging of the breast. IEEE Trans. Microw. Theory Tech. 48, 1841–1853 (2000).
10. Li, D., Meaney, P. M. & Paulsen, K. D. Conformal microwave imaging for breast cancer detection. IEEE Trans. Microw. Theory Tech. 51, 1179–1186 (2003).
11. Crocco, L. & Vipiana, F. An Innovative Framework for Advancing Microwave Medical Imaging: The EMERALD European Network. 13th Eur. Conf. Antennas Propagation, EuCAP 2019 (2019).
12. Meaney, P. M. et al. Microwave imaging for neoadjuvant chemotherapy monitoring: Initial clinical experience. Breast Cancer Res. 15, R35 (2013).
13. Crocco, L., Di Donato, L., Catapano, I. & Isernia, T. The factorization method for virtual experiments based quantitative inverse scattering. Prog. Electromagn. Res. 157, 121–131 (2016).
14. Colton D. & Kress R. Inverse Acoustic and Electromagnetic Scattering Theory. Berlin, Germany: Springer-Verlag,1992
15. He, K., Sun, J. & Tang, X. Guided image filtering. IEEE Trans. Pattern Anal. Mach. Intell. 35, 1397–1409 (2013).
16. Andreuccetti, D. & Fossi, R. Dielectric Properties Of Human Tissues: Definitions, Parametric Model, Computing Codes. 34 (2000).
17. Jaccard, P. the Distribution of the Flora in the Alpine Zone. New Phytol. 11, 37–50 (1912).