

Detecting Pathological Changes in the Brain Due to Alzheimer Disease Using Numerical Microwave Signal Analysis

Rahmat Ullah ^{*1}, Tughrul Arslan ^{*2}

^{*} School of Engineering, University of Edinburgh
Kings Buildings, Edinburgh, EH9 3FF, United Kingdom

¹ rahmat.orakzai@ed.ac.uk

² tughrul.arslan@ed.ac.uk

Abstract—Microwave techniques are being investigated to detect various biological conditions such as cancer, stroke, and neurodegenerative disorder due to ease of accessibility and lower cost. This paper presents initial results on the use of microwave signal analysis for the detection of Plaque and tangles changes in the brain caused by Alzheimer's disease. Various brain phantoms are created using a commercial microwave design suite to mimic different stages of Alzheimer especially pathological changes caused by beta-amyloid plaques and tau tangles in the brain. These phantoms are penetrated with an array of six monopole directional antennas and the reflected signals are stored and analysed. Numerical signal analysis for different stages of Alzheimer disease shows that there are significant variations due to Plaque and tangles in the brain. These preliminary results also show that microwave imaging can be used for the detection of Alzheimer disease at initial stages.

Index Terms—Alzheimer disease, brain Imaging, CST Simulations, dielectric properties, microwave signal analysis

I. INTRODUCTION

Alzheimer disease (AD) is a common neurodegenerative disease that affects cognitive functions and behaviour due to cognitive decline. This disease, which frequently occurs among the elders, has a very long preclinical phase (approximately 20 years), and a clinical duration of nearly 8–10 years [1]. It affects the structure and functions of neurons, which leads to the death of neurons. At present, the morbidity of Alzheimer's disease is increasing every year. The morbidity of the elderly aged 65–80 is more than 5% worldwide, and the morbidity of the elderly aged over 80 is more than 20%. There is no clear conclusion on the pathogenesis of AD at present, that may be caused by the lack of acetylcholine [2].

According to the Alzheimer's Society, there are over 520,000 people with dementia caused by AD. These numbers are expected to increase to 1 and 1.6 million by 2025 and 2040 respectively and would cost £94.1 billion for patient care [3]. Unfortunately, although medicines are available that can help relieve some of the symptoms, there is currently no cure for AD. Therefore, it is crucial to detect AD at earlier stages, to stop or slow its progression.

Pathological changes in the brain caused by AD include brain atrophy, shrinking of the hippocampus, and lateral ventricle enlargement, as well as an increase in the cerebral spinal fluid (CSF) [4]. However, another significant change in the brain caused by AD is the gradual accumulation of beta-amyloid plaques and tau tangles in the brain regions, linked to memory [5]. Beta-amyloid proteins in the AD affected brain stick together in irregular clumps to form plaques among neurons. It interrupts the signals amongst synapses and obliterates a vital cell transport system made

of proteins. Besides, neurofibrillary tangles are increased with the progression of AD. These tangles are disjointed cytoplasmic filaments caused by tau proteins that stabilise microtubules in the brain. This declines the microtubules, affecting the ability of the brain to transport cell nutrients and finally leads to the death of neurons [6]. These plaques and tangles are formed in the hippocampus region and gradually spreads to other regions of the brain as shown in Fig. 1.

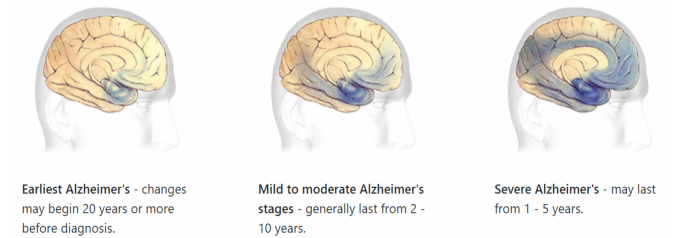


Fig. 1. blue-shaded areas show plaques and tangles that spread through the entorhinal cortex as AD progresses. The progression rate varies significantly from patient to patient (From Alzheimer's Association [7]).

Traditional imaging modalities such as Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) are being used to detect the changes in the brain. It can provide information about the shape, location, and size of malignant brain tissue. However, they have many limitations. CT entails a higher dose of ionising radiations in addition to being slower and more complex [8]. Furthermore, it exposes patients to ionising radiation which enhances the risk of cell mutation. Conversely, MRI generates high-quality images with better spatial resolution and is better suited for imaging soft tissues (e.g. to differentiate between white matter and grey matter). The downside of MRI includes high equipment cost, system complexity, and time required for data collection. One scan of MRI lasts for about 05 minutes. Moreover, MRI is not appropriate in various other situations such as patients with a heart pacemaker, as magnetic fields can disrupt the operation [9].

Microwave imaging is a potential imaging method being studied for various biomedical applications especially breast and brain-related diseases. It is non-ionising with emission power less than a cell-phone radiation. Additionally, its portable and wearable nature makes it more convenient for patient's use [10]. The disadvantage is it does not produce high resolutions images, compared to the CT or MRI. However, owing to its advantages, several research groups are working on the improved antenna and wearable structure design, pre-processing and imaging algorithms, scattering

techniques, and validation of these imaging methods [11].

This study aims to investigate if changes caused by Plaques and tangles inside the brain, could be detected through numerical microwave signal analysis. For this purpose, different brain phantoms were created using CST Studio Suite to mimic the different stages of the AD affected brain. Measurements were taken using an array of six monopole antennas and were analysed for trends that correlate to the changes due to plaques and tangles. It is a challenging problem; since the response from small changes in the brain is hidden, in the cumulative response of different layers of head such as skin, skull, and CSF. The solution relies upon inferring the relationship among the magnitude of reflected signals and the dielectric properties at brain functional site. Numerical analysis and imaging is performed to distinguish major stages of AD based on the changes in the reflected signals.

II. MODELING HEALTHY AND AD BRAIN

In our previous work, it was found that there exists a major change in the dielectric properties in healthy and AD affected brain [12]. The dielectric properties affect how the electromagnetic signals transmit, reflect, and are absorbed in biological tissues. The study shows that at 770 MHz, the relative permittivity for grey matter is 53.3, and 45.3 for a healthy and AD affected brain, respectively. It indicated that there is a 15% decrease in the relative permittivity for the AD brain. Similarly, at 770 MHz frequency, the conductivity for grey matter is 0.8906 S/m and 1.6253 S/m for the healthy and AD-infected brain, which indicated an increase of 82.5%.

The effect of plaque and tangle on the white matter reveals similar results. For example, at 770 MHz the relative permittivity for white matter is 39.35 and 32.57 for healthy and AD-infected brain, respectively, which indicates an increase of 17.61%. Likewise, at 770 MHz, the conductivity for white matter is 0.554 S/m for healthy and 0.702 S/m for the AD affected brain, indicating an increase of 26.72% in the conductivity.

These observations suggest that it may be possible to detect AD by monitoring the changes in the plaque and tangle at the early stages of the disease. For the purpose, different brain phantoms are created by utilizing this information. CST microwave studio is used to create realistic human head phantoms to mimic the healthy and AD affected brain, that consists of skin, skull, CSF, blood, white matter, and grey matter. Four different realistic head models are created to reflect the stages of AD inside the brain. A model along with six surrounding antennas can be seen in Fig. 2. Dielectric values from our previous work were used to mimic mild, moderate, and severe stages of AD. A model of the healthy human brain was created to compare the results with AD brain models. This detailed phantom creation, while time-consuming, enables to investigate the change in the brain caused by beta-amyloid plaques and tau tangles.

An array of six monopole directional antennas is used to penetrate these models. The antenna design is based on a rectangular planar monopole structure. The directionality of the antenna was ensured by conducting far-field simulations to calculate the front-to-back (FTB) ratio. The simulated FTB ratio of the used antenna is 6 dB at its central frequency of 2.5

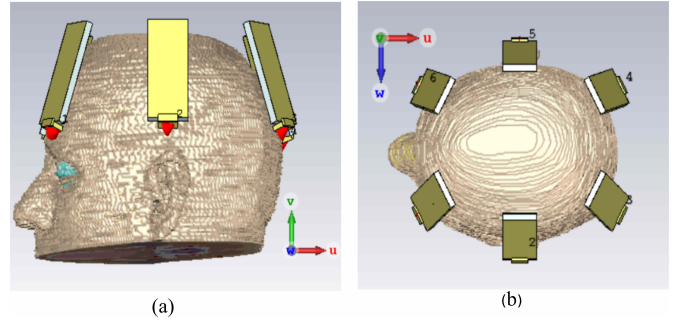


Fig. 2. (a) Front view and (b) Top View of Brain phantom and six surrounding antennas.

GHz, which confirms its directional property. Moreover, numerical simulations conducted for E-field show that it offers good penetration depth inside the head. This is essential to ensure the antenna's ability to probe inside the head to detect small changes. More information on the antenna used can be found in [13]. These antennas are placed around the models with an equal distance covering the whole head model. In order to ensure good penetration, a working frequency of 0.5 to 5 MHz was used. Finally, the simulations were performed to capture the reflected signals (S11) for all antenna and all cases. The total number of 1001 frequency points were stored for each antenna. These points were organized as a matrix for each case and analysed for variations due to the change in dielectric properties for each case.

III. RESULTS AND ANALYSIS

The reflected signals were imported to matrix laboratory (MATLAB) for further analysis. Fig. 3 shows the reflected signals from all antennas for each case against the working frequency from 0.5 to 5 GHz. It was found that between 3 to 5 GHz, the electromagnetic wave reaches the region associated with plaques and tangles in the brain. Furthermore, significant variations among the reflected signals can be seen due to the change in the dielectric properties.

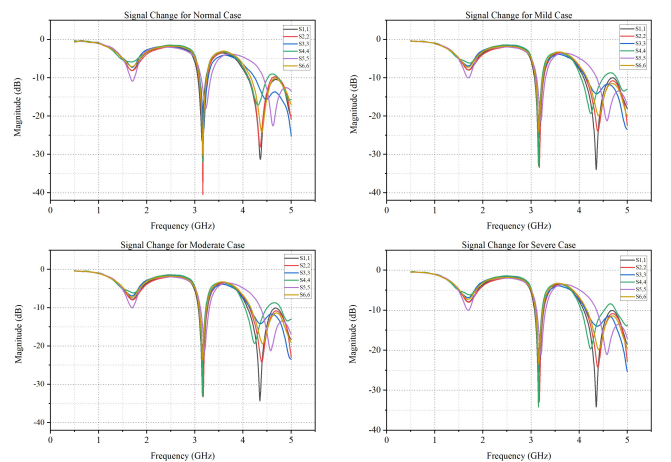


Fig. 3. Reflected signal from a healthy, mild, moderate, and severe case of human brain phantom using an array of six antennas. More signal loss can be observed from 4 to 05 GHz of the frequency range, due to increase in plaques and tangles

These reflected signals are compared to the signal received from a normal (healthy) brain phantom. It can be noted from

Fig. 3 that there is a significant variation among signals from 4 to 5 GHz of the frequency range. There is an overall downward shift in the reflected signal which indicates the signal loss as they are not reflected due to the higher dielectric difference from mild to severe brain tissues. Antenna located near the hippocampus region show more loss in the reflected signals. For instance, at 4.35 GHz the values for Antenna 1 is -30.67, -33.98, -34.17, and -34.32 for a normal, mild, moderate, and severe case, respectively. Furthermore, it can be observed that there is no change in the characteristics of reflected signals from 0.5 to 3 GHz for the normal and severe stages of AD. These results ensure that the change caused by plaque and tangle could be detected by using non-invasive microwave signals in a suitable operating frequency range.

To investigate the cumulative change, effect size (ES), percent change (PC) and P-value are used as quantitative measures for the magnitude of reflected signals from all antennas. ES is calculated by the ratio of mean difference in two groups divided by the standard deviation of the control group (healthy brain data). PC is calculated by using the following formula

$$PC = \frac{(TG_m - CG_m)}{CG_m} * 100 \quad (1)$$

Where TG_m is test group mean and CG_m represents the control group mean. The results are shown in Fig. 4. The higher values for severe case indicate a larger difference between normal and severe AD. There is also a small difference between mild and moderate cases due to the small amount of changes in the brain. Furthermore, the p-value for the mild, moderate, and severe cases is 1.57683E-4, 2.38792E-4, 2.66533E-4 respectively. The significance value of p was chosen to be at 0.05. Hence the p-value is smaller than 0.05, therefore it can be concluded that the population mean for all cases are significantly different.

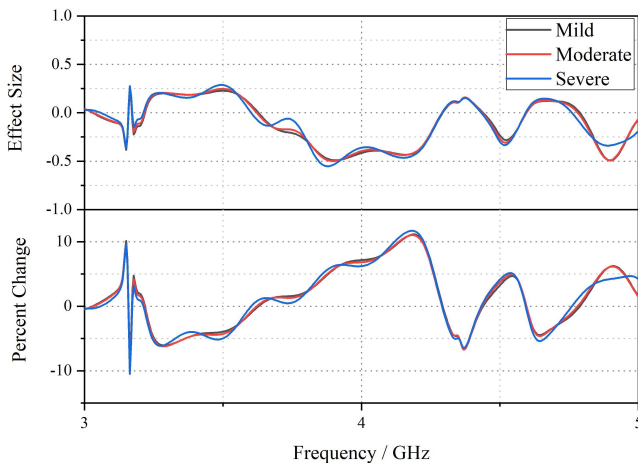


Fig. 4. Effect size and percent change values for all cases calculated with respect to normal Case. The higher values represent a larger difference to the control group.

The statistical analysis of the reflected signal reveals a direct relationship among the severity of plaque and tangle with increase loss in the reflected signals. To validate these results, these reflected data are used to reconstruct the images using an optimized algorithm proposed in our previous work

[8]. The signals from brain tissue are partly reflected and partly absorbed. The magnitude of reflected signals are used for image reconstruction. These signals are first converted to time domain using Inverse Fast Fourier transform. According to the proposed algorithm, each reflected signal is thoroughly delayed and filtered to remove clutter. The processed signals are then accumulated to obtain the energy values for the entire imaged tissues. The results for all cases can be seen in Fig. 5.

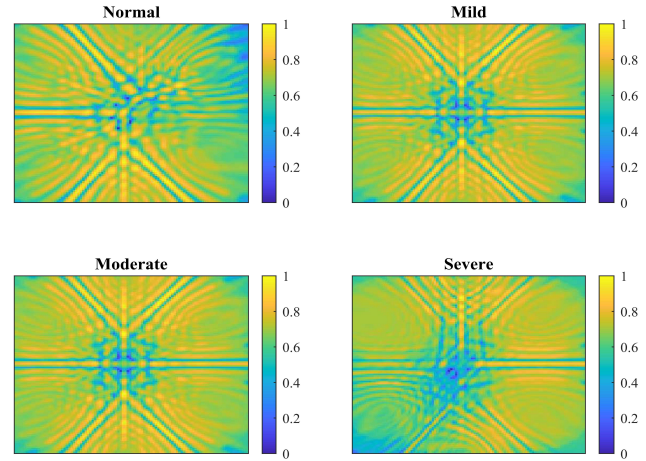


Fig. 5. Imaging results for all cases. Energy is accumulated for all six antennas. There is less difference between mild and moderate case. A decrease in energy at the center can be seen from normal to severe case (where more signals are absorbed)

It can be noted that the energy from normal to severe case decrease, indicating more loss in the signal as they do not get reflected. Furthermore, there is an insignificant change in the mild and moderate cases which further strengthens the statistical analysis results. This meant that with an increase in plaque and tangles, more signals were absorbed by the tissues in the brain area. The low energy region from mild to severe cases are getting relatively smaller in the middle area. In principle, the change in the dielectric properties in different cases absorbed signals and refracted them. These results validate that AD can be detected at early stages using low cost and non-invasive microwave approaches.

IV. DISCUSSION

Alzheimer's disease causes the death of neurons that gradually lead to tissue loss throughout the human brain. Various changes in the brain affected by AD are being studied and it is believed that the plaques and tangles are the primary suspects. The detection of these small changes is a challenging problem, since the response from small changes in the brain is hidden, in the cumulative response of different layers of head. This work investigate the use of microwave signal for the detection of these small changes. The mechanism of the detection approach is analysed by deducing the relationship among the magnitude of reflected signals and dynamic dielectric properties of the targeted area. The change in the dielectric properties at functional site due to plaques and tangle, affects the signal propagation. The electromagnetic signals either reflects, transmits or absorbed in the brain tissue based on its dielectric properties. The simulation performed on realistic head models reveal that

with the progression of AD, more signals are absorbed in the hippocampus. It cause an increase in the loss of reflected signal, due to the higher dielectric properties of plaques and tangles compared to other brain tissues. The results shows that, signal from Antenna 1, 2, 5 and 6 indicated more loss as they are located near the cortex. Statistical analysis for all antenna ensure that there is signal loss in the commutative response. As a result, the calculated energy values, decrease gradually from normal to severe case. The signals from all antennas in the resulting image is clearly visible, however the signal are distorted. The numerical and imaging results can be improved by using more number of antennas. It is also important to mention that no signal subtraction is performed for the imaging algorithm. The skin and skull characterize the penetration depth in the microwave head imaging. Therefore, it is a common practice to subtract the signals received from an empty head model to eliminate the strong reflection from skull. The propagation inside the brain tissue is also dependent on the frequency range. Lower frequency signal provide better and deeper penetration, however it decreases the spatial resolution of output image. Therefore, it is important to choose a suitable range of frequency, precise setup, number of antennas and optimized antenna location for detecting small changes in the brain.

V. CONCLUSION AND FUTURE WORK

To detect Alzheimer's disease using numerical microwave signal analysis, different brain phantoms were created to mimic the stages of the disease. An array of six antenna was used to detect the changes in the brain due to changes in dielectric properties of the brain caused by Alzheimer's disease. The numerical results show significant loss in the magnitude of reflected signals from healthy to severe cases. The imaging results also shows energy loss, that verify the numerical results. consequently, it can be concluded that numerical microwave signal analysis alone can be used to detect small changes in the AD affected brain. Both numerical and imaging results verify the effectiveness and feasibility of using microwave to detect the changes in the brain caused by AD using microwave reflected signals. In the future, further investigations will be performed using more antennas and in-vivo validation of the results to detect these variations. These initial investigations could lead to a non-invasive approach to detect AD at initial stages. Detecting the changes in the brain at earlier stages of AD will give physicians very powerful tools to help detect rapidly advancing diseases in less time.

REFERENCES

- [1] M. G. Ulep, S. K. Saraon, and S. McLea, "Alzheimer disease," *The Journal for Nurse Practitioners*, vol. 14, no. 3, pp. 129–135, 2018.
- [2] E. Dallé, M. V. Mabandla, and W. M. Daniels, "Dielectric constant and conductivity of blood plasma: Possible novel biomarkers for alzheimer's disease," *Oxidative Medicine and Cellular Longevity*, vol. 2020, 2020.
- [3] "Publications and factsheets: Full list," 2020, last accessed 16 May 2020. [Online]. Available: //https://www.alzheimers.org.uk/get-support/publications-factsheets-full-list
- [4] C. Reitz and R. Mayeux, "Alzheimer disease: epidemiology, diagnostic criteria, risk factors and biomarkers," *Biochemical pharmacology*, vol. 88, no. 4, pp. 640–651, 2014.
- [5] C. R. Harrington, "The molecular pathology of alzheimer's disease," *Neuroimaging Clinics*, vol. 22, no. 1, pp. 11–22, 2012.
- [6] C. Ballatore, V. M.-Y. Lee, and J. Q. Trojanowski, "Tau-mediated neurodegeneration in alzheimer's disease and related disorders," *Nature Reviews Neuroscience*, vol. 8, no. 9, pp. 663–672, 2007.
- [7] "Alzheimer's association," 2020, last accessed 23 May 2020. [Online]. Available: https://www.alz.org/alzheimers-dementia/what-is-alzheimers/brain-tour
- [8] R. Ullah and T. Arslan, "Pyspark-based optimization of microwave image reconstruction algorithm for head imaging big data on high-performance computing and google cloud platform," *Applied Sciences*, vol. 10, no. 10, p. 3382, 2020.
- [9] R. Chandra, H. Zhou, I. Balasingham, and R. M. Narayanan, "On the opportunities and challenges in microwave medical sensing and imaging," *IEEE transactions on biomedical engineering*, vol. 62, no. 7, pp. 1667–1682, 2015.
- [10] I. Saied, S. Chandran, and T. Arslan, "Integrated flexible hybrid silicone-textile dual-resonant sensors and switching circuit for wearable neurodegeneration monitoring systems," *IEEE transactions on biomedical circuits and systems*, 2019.
- [11] M. Islam, M. Mahmud, M. T. Islam, S. Kibria, and M. Samsuzzaman, "A low cost and portable microwave imaging system for breast tumor detection using uwb directional antenna array," *Scientific reports*, vol. 9, no. 1, pp. 1–13, 2019.
- [12] I. Saied, M. Bashri, T. Arslan, C. Smith, and S. Chandran, "Dielectric measurements of brain tissues with alzheimer's disease pathology in the microwave region," in *2019 IEEE International Symposium on Medical Measurements and Applications (MeMeA)*. IEEE, 2019, pp. 1–6.
- [13] I. Saied and T. Arslan, "Wideband textile antenna for monitoring neurodegenerative diseases," in *2018 IEEE 29th Annual International Symposium on Personal, Indoor and Mobile Radio Communications (PIMRC)*. IEEE, 2018, pp. 356–360.