Millimeter-Wave Systems for Real-Time Intraoperative Brain Tumor Resection Assistance

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Abstract: Brain cancer is one of the deadliest forms of cancer due to limited treatment options and challenges in tumor differentiation during surgery. Current surgical assistance tools, such as intraoperative imaging systems and advanced visualization techniques, often face limitations in cost, accessibility, and precision. Microwave and millimeter-wave (mmWave) technologies have emerged as promising alternatives for real-time, non-invasive differentiation of healthy and cancerous brain tissues, leveraging their sensitivity to dielectric property variations. This paper reviews the state-of-the-art microwave and mmWave systems developed for medical diagnostics, focusing on brain tumor detection. It highlights their underlying principles, performance, and limitations while discussing their potential to address the drawbacks of existing tools. By analyzing recent advancements, the review identifies key areas for future development, proposing characteristics of an ideal system to support real-time surgical decision-making. Additionally, the paper proposes a system designed to measure the dielectric properties of the brain tissue, aiming to enhance real-time surgical decision-making and improve patient outcomes.

1 INTRODUCTION

The last GLOBOCAN report showed that in 2022 there were nearly 20 million new cancer cases and that almost 10 million deaths were caused by it, meaning that one in five individuals can potentially develop cancer throughout their lives. Despite ranking nineteenth in new cases, brain cancer has limited treatment options available, making it one of the most devastating prognoses, often fatal (Bray et al., 2024).

According to the available data, brain cancer has a 5-year relative survival rate of 33.4%, which drops to less than 10% for the most aggressive brain tumors, such as glioblastomas (*Brain and Other Nervous System Cancer — Cancer Stat Facts*, 2020). To try and help cure the brain tumor, as of today, the main treatments used are radiotherapy and surgery, craniotomy being the most common surgery in this case. In this surgery, a neurosurgeon cuts out an area of bone from the skull exposing the dura mater. After the cut and removal of this tissue, a part of the brain is exposed, and the resection of the tumor is possible (*Surgery for Brain Tumours - Cancer Research UK*, 2023).

Despite being an area in constant evolution, surgery is often insufficient to provide a permanent cure for some of the most aggressive tumors, like high-grade gliomas and medulloblastomas (Delaidelli & Moiraghi, 2024). Many times it is not possible to remove the full mass of the cancer leaving behind some parts of it, given that distinguishing the tumor from the surrounding healthy tissue is not an easy task (Delaidelli & Moiraghi, 2024; *Surgery for Brain Tumours - Cancer Research UK*, 2023). Usually, the surgeon has to use expertise and previous knowledge to decide if the tissue is healthy or malignant. Studies show that 80% to 90% of tumor recurrence has origin in an incomplete resection (Petrecca et al., 2013).

Even though the diagnostic techniques for brain tumor detection have an extended characterization,

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real-time intraoperative information still needs more development, especially in tumors where the main treatment is the maximal removal of the mass. There are several techniques and tools to help neurosurgeons remove tumors, however, they come with some drawbacks and limitations.

Tools like the exoscope, which is based on positioning a camera alongside the surgeon, offering two to three-dimensional high-resolution imaging on a display monitor placed in front of the surgeon, presents a learning curve for surgeons accustomed to traditional microscopes, leading, in some cases, to the change to the conventional operating microscope during the surgery and has some substantial costs (acquisition and maintenance), which may not be feasible for all healthcare settings (Ariffin et al., 2019; Montemurro et al., 2021).

The Fluorescence-guided surgery technique provides real-time intraoperative tumor visualization by using selective fluorescence compounds in tumor cells to delineate cancer tissue during surgery (Hadjipanayis et al., 2015). Nevertheless, it can still cause some interpretation errors, is not available for all types of brain cancer, and also necessitates the use of specialized surgical visualization systems, resulting in more costs for the hospital (Su et al., 2014).

Raman spectroscopy works by directing a single-wavelength light beam onto a sample and observing the scattered light as it interacts with the molecules within the sample. However, this technique has a weak intensity signal and long data acquisition and processing times (Rivera et al., 2024).

The use of confocal microscopy, a technique that creates a point source of light and eliminates out-of-focus light, enabling high-resolution imaging deep into tissues and optical sectioning for 3D reconstructions, may blur and overlap regions of hypercellularity, reducing confidence in the classification (Elliott, 2020).

The more conventional intraoperative imaging approaches, such as intraoperative magnetic resonance imaging (iMRI) and intraoperative computed tomography (iCT), have lengthy image acquisition times and require the interruption of the surgery, which translates into longer surgeries and more time under anesthesia for the patient. Additionally, these techniques are quite expensive and are not available in most healthcare facilities.

The intraoperative ultrasound (iUS) normally does not have enough spatial resolution for the detection of microstructures or cellular elements.

With this, it is clear that there is a need for a way to differentiate tissue during brain tumor resection surgery that works in real-time, *in situ* and is low-cost. Radiofrequency (RF) technology has shown an increasing potential in the medical and healthcare field because tumors and normal tissues have different dielectric properties due to their different tissue structure and vascularization, and generally, cancer cells have a higher water content (Wang et al., 2024). The RF short wavelengths may allow for the achievement of higher spatial resolution, making them very effective for sensing pathological changes.

Over the years, significant progress has been made in characterizing the dielectric properties of biological tissues, particularly up to 20 GHz. However, studies on the dielectric properties of human tumor tissues remain limited. This scarcity is largely due to challenges in conducting measurements, including the complex logistics of systematic sample collection, proper handling, and timely testing within hospital environments. These practical constraints have hindered the comprehensive study of tumor tissue dielectric characterization. Additionally, the dielectric properties of intracranial tumors appear to be depending on histological class and malignancy grade, showing significant intratumoral heterogeneity (Kordić & Šarolić, 2023).

Nevertheless, Table 1 presents some of the results reported in the literature, with the values calculated separately for the real ($\boldsymbol{\varepsilon}_r'$) and imaginary ($\boldsymbol{\varepsilon}_r''$) parts of the measured permittivity as a percentage difference, offering a concise overview of the dielectric properties of tumor tissues.

Table 1: The average discrepancy in permittivity between tumor tissues and their surrounding tissues is provided, along with the temperature and frequency ranges reported in the studies.

Authors	**Tumor Tissue**	$\boldsymbol{\Delta\varepsilon_r'}$ **(%)**	$\boldsymbol{\Delta\varepsilon_r''}$ **(%)**
(Lu et al., 1992)	Glioma in comparison to white matter (0.005–0.5 GHz)	30	30
(Kordić & Šarolić, 2023)	Meningioma in comparison to white matter tissue (0.5–18 GHz)	76.7	157.6
	Meningioma in comparison to gray matter tissue (0.5–18 GHz)	11.6	16.7

To obtain values for dielectric properties above 20 GHz, empirical models can be employed, such as the one proposed by Schepps and K. Foster (Schepps & Foster, 1980). Figure 1 shows the dielectric properties for both healthy brain tissue and brain cancer tissue, providing a comparative analysis at higher frequencies.

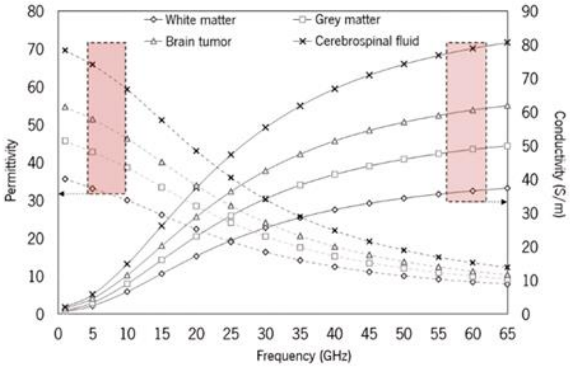

Figure 1: Representation of the variation in dielectric properties, including conductivity and permittivity, calculated for the various constituents of the brain and brain tumor as a function of frequency (Cardoso, 2019).

2 RF-BASED DETECTION OF TISSUES: POTENTIAL AND CHALLENGES

Microwaves represent a form of electromagnetic radiation characterized by frequencies that vary from 3 GHz to 30 GHz. Various electromagnetic measurement methods and imaging techniques have been utilized on biological tissues since the different dielectric properties between healthy tissues and cancerous tumor tissues have raised optimism about employing microwaves for medical diagnostic purposes.

With this, several studies and works have been conducted on diagnostic tools, both with and without contact, as well as imaging techniques using microwaves (Çalışkan et al., 2015; Raihan et al., 2017; Zhang et al., 2013). Most of these tools were developed to detect specific healthy or cancerous tissues, such as tumors. The main concept behind using microwaves for diagnostics is the use of transmitting antennas to emit electromagnetic waves and receiving antennas to capture the scattered waves, enabling the detection or distinction of certain tissues (Çalışkan et al., 2015). Since different tissues absorb varying amounts of energy due to their differing dielectric properties, such as electrical conductivity (σ) and relative permittivity (ε_r), these properties play a crucial role in identifying different tissue types.

The primary advantages of using microwaves in diagnostic tools include the harmless nature of this type of radiation when used at low levels and its relatively low cost, even for more complex systems, when compared to iCT or iMRI. Additionally, the availability of a relatively wide frequency range is a significant benefit of using these techniques (Rosen et al., 2002). However, despite the fact that RF waves do not possess the resolution necessary to visualize microstructures or surpass the resolution of iUS, the latter uses systems of 4 to 10 MHz approximately, which translates into larger probes, difficult to insert in the small craniotomy hole. This can be overturned by the use of higher frequencies, since it is possible to develop antennas with small physical dimensions allowing for smaller devices.

In 2019, (Alqadami et al., 2019) proposed a “Wearable Electromagnetic Head Imaging System utilizing a Flexible Wideband Antenna Array Based on Polymer Technology for Brain Stroke Diagnosis”. The system features eight high-efficiency, flexible, lightweight, and robust antennas, designed specifically for stroke applications. Scanning and image reconstruction are completed in just 8 seconds. The antennas offer a 54% fractional bandwidth (1.16-1.94 GHz) and over 80% radiation efficiency, satisfactory wave penetration in head tissues.

(Chowdhury et al., 2017) designed a wearable pentagon-shaped antenna for brain tumor detection in a compact form to be placed on the patient's head. It was specifically developed to detect tumors at an early stage. The antenna achieved satisfactory results, demonstrating a frequency shift of 18 MHz in the resonance frequency between a normal head and a head with a tumor. The bandwidth of the proposed antenna was 2.4-2.4835 GHz.

(Mohammed et al., 2014) suggested a microwave imaging system capable of producing brain images to identify the position and extent of brain injuries, such as strokes, with a bandwidth of 3 GHz (1-4 GHz). The system features a semi-elliptical array of 16/32 antenna elements mounted on an adjustable platform, a data acquisition unit, a Vector Network Analyzer (VNA), and a computer. It offers portability and executes scans in 20 seconds. Specifically designed for stroke detection, the system accurately identifies the presence of a stroke and predicts its location within a margin of a few millimeters.

A common problem of the systems previously described is their size. None of the systems are adequate for use during surgery, especially considering the small opening created by the surgeons to access the brain tumor for resection.

A way to address this issue is the use of higher frequencies, such as millimeter waves (mmWave). Because of the small wavelength, mmWave devices facilitate large antenna arrays packed in miniature physical dimensions, allowing for packing more antenna elements at mmWave frequencies than at microwave frequencies, resulting in a narrower beam and increased resolution (Chittimoju & Yalavarthi, 2021).

The short wavelengths of mmWave allow for the achievement of higher spatial resolutions at the cost of reduced penetration depths (600 µm to 1.2mm into the body), making them very effective for sensing pathological changes in different skin layers or the outer tissue layers of excised organs (Mirbeik-Sabzevari et al., 2018). Furthermore, existing mmWave technologies have demonstrated a significant decrease in unnecessary biopsies, indicating a potential pathway for continued research on non-invasive early cancer screening in the future. Such technologies and systems are going to be shown in the next section.

3 APPLICATIONS OF mmWAVE TECHNOLOGY IN MEDICAL DIAGNOSIS AND TREATMENT

Over the years, there have been developed some prototypes of systems and tools that use mmWave for medical diagnostics and has been studied the potential therapy effects of these waves. In this section, some of these prototypes will be shown, as well as the setup used and the potential limitations of each.

(Töpfer et al., 2015) proposed a miniaturized broadband mmWave near-field probe with a conical probe tip, designed to operate at frequencies between 90 and 104 GHz, for skin cancer identification. The probe utilizes a dielectric waveguide with a high-resistivity silicon core, with the sensing end tapered into a conical tip. This tapering focuses the electric field into a small area, enhancing the probe's lateral resolution. Since the dielectric properties of the skin vary between individuals and across different body locations, the probe performs differential measurements, i.e., the signal from a suspicious area is compared with the surrounding tissue, enabling the probe to detect subtle differences that may indicate the presence of cancer. For the s-parameter measure, the waveguide was connected to a VNA with mmWave extension heads to 110 GHz through a coaxial adapter. The network analyzer was calibrated by thru-reflect-line (TRL) or one-port calibration using WR-10 waveguide standards at the coax-to-waveguide adapter output plane.

The probe demonstrated high responsivity at 96 GHz, with an S11 change of 1.83 dB for a tip size of 0.6 mm × 0.5 mm, and a sensing depth of 0.3–0.4 mm. The long-term measurement stability was 0.66% over 8 hours, ensuring consistent and reliable performance.

Still in skin cancer detection, a novel multi-tone mmWave radar sensor was presented (Arab et al., 2020). It is based on a low-cost Miniature Hybrid Microwave Integrated Circuit design (MHMIC) at 77 GHz. The proposed radar system uses a six-port interferometer with I/Q demodulation to recover information. It employs a linear passive mmWave circuit with four 90° hybrid couplers and a phase shifter, fabricated on a ceramic substrate using MHMIC technology. An 8×2 microstrip patch antenna array is utilized for enhanced performance and coverage. In the measurement setup, the source frequency is set to 12.83 GHz with a 10 dBm power output and the multiplier will generate a 77 GHz signal with 0 dBm power at the input of the parallel line coupler.

This sensor had promising results, showing that it was able to distinguish between dry hand skin, wet hand skin and water. However, these results are with a limited number of samples, needing more to represent the diversity of the human skin better. Additionally, the calibration steps are not mentioned, which are crucial for an accurate measure.

(Mansutti et al., 2020) proposed and designed a probe for early skin cancer detection. The measurement setup consists of connecting the probe to the VNA via a high-frequency cable and mounted on a Computer Numerical Control machine, used to determine the correct height of the probe for measurements, ensuring direct contact with the surface material under test. The measurement procedure involves scanning the probe over a 2D grid with a 1 mm step size in both directions, acquiring data from multiple points on the skin model since an imaging algorithm is intended to be applied, to generate tissue structure maps. The resonance frequency obtained was nearly 40 GHz and a lateral sensitivity and detection depth of 0.2 mm and 0.55 mm respectively.

The mmWave technology is also used for the development of imaging systems (Chao et al., 2012). The article proposes a method for breast cancer imaging using quasi-optical free space mmWave spectroscopy, generating 2D and 3D tissue structure maps to differentiate normal tissue from cancerous tissue. The measurement setup employs a quasi-optical free space mmWave spectrometer with tunable backward wave oscillators operating in the 30-120 GHz range. Key components include an isolator, modulator, horn antennas, focusing lenses, and a Schottky diode detector. Despite the proposed system being capable of the referred 2D and 3D tissue structure maps, the relatively large diameter of the energy beam used in the measurement limits the spatial resolution of the image and the low power of the mmWave used limits the depth penetration.

Still in the use of mmWave for imaging systems, (Mirbeik et al., 2022) developed a high-resolution mmWave imaging system for skin cancer detection. The system comprises a set of antennas designed to transmit and receive mmWave within a specific frequency band optimized for skin imaging. These antennas, using an ultra-wide synthetic bandwidth of 98 GHz (12-110 GHz), achieved by integrating two sub-bands, scan the target skin area by emitting mmWave and capture the reflected signals. The antipodal Vivaldi antennas ensure perfect impedance matching and stable gain across the frequency range, enhancing the system's performance during scanning. To further improve precision, the system incorporates a motorized XYZ linear arm, enabling 3D scanning of the target area. The data collected is processed using a reconstruction algorithm that leverages the dielectric properties of various tissue types to generate detailed images, highlighting cancerous tissue areas with high accuracy. Additionally, the system operates in real-time, completing each measurement in approximately 20 seconds, which minimizes patient discomfort and mitigates the effects of movement during the procedure. However, despite the good results obtained, the system's performance was not consistent across all skin lesion classes.

4 PROPOSED mmWAVE SYSTEM

Based on prior knowledge and advancements in mmWave technologies, a system is proposed (Figure 2) to differentiate biological tissues based on the dielectric properties. The system operates with mmWave technology and is structured into several key components, such as a signal generator (Agilent 83623B), a frequency multiplier (HAFMV4-187), a mixer (QMC-MXB15-NBMCA), and a custom probe developed in-house (Cardoso, 2019). The signal generator produces an initial signal that is upconverted to higher frequencies through a multiplier. The signal generator produces a 13 GHz continuous wave that is converted to 52 GHz through the 4x multiplier, which is used as the local oscillator (LO) of the mixer. The signal from the VNA (Keysight E5071C), with a proposed frequency of 2 GHz, is the intermediate frequency (IF) and it will be upconverted in the mixer, resulting in a 54 GHz signal. After filtering (SWF-50346340-15-H1), this signal is transmitted from the probe to interact with the material under test (MUT).

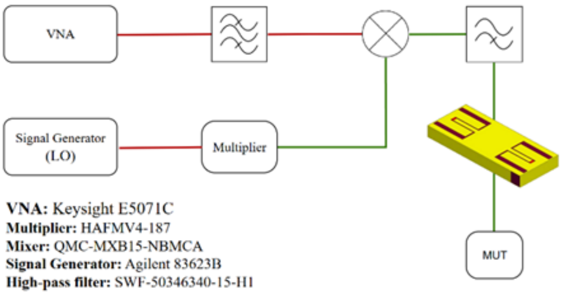

Figure 2: Proposed mmWave system setup. Red lines represent microwave signals, while green lines represent mmWave signals.

The reflected signals are measured and analyzed using the VNA, which calculates the S-parameters. These parameters provide insights into the dielectric characteristics of the MUT, enabling real-time detection of changes in the tissue.

The proposed system's architecture allows for modular testing and optimization of the components, ensuring flexibility for adjustments in the frequency range, signal power, or filtering capabilities. Additionally, the combination of high-frequency operation with precision measurement tools should ensure reliable and repeatable results, crucial for intraoperative applications.

The primary objective of this system is to test if it is possible to adapt the existing equipment and a VNA to detect subtle variations in tissue properties, such as those between healthy and abnormal brain tissue. To do this, human body phantoms with different dielectric properties will be made, and it will be attempted to distinguish them with the proposed setup by analyzing the signal reflected by the phantom, in order to validate and obtain the system sensibility, i.e, the minimum detectable change in dielectric properties that allows the differentiation between healthy and tumor tissues. The human body phantoms will be created with mixtures of deionized water, Triton X-100 and diethylene glycol butyl ether (DGBE), an alcohol, to test the system, as these are standard ingredients for human body phantom development (FCC, 1997).

It is expected that this system will pave the way for the development of a stand-alone mmWave brain tumor detector, as it will serve as an adaptable platform to test different components and system architectures.

5 CONCLUSIONS

This study highlights the potential of mmWave technology for intraoperative applications, particularly in distinguishing brain tissues during oncological procedures. By leveraging the different dielectric properties of tissues, mmWave systems have demonstrated a capacity to provide accurate and real-time feedback that can significantly assist surgeons in differentiating between healthy and tumor-affected regions. This approach addresses the limitations of current imaging technologies, such as low resolution or time delays, and offers a precise tool for surgical guidance.

The use of mmWave frequencies is particularly advantageous because the small wavelength enables compact component design and high spatial resolution, which are critical for detecting subtle variations in tissue properties in a confined surgical environment.

Based on the findings of the literature review, we propose a system that, employing a VNA, aims to study the possibility of detecting subtle variations in tissue properties, in order to obtain the minimum detectable change that allows the differentiation of tissues. The next steps will focus on developing a fully functional mmWave system for intraoperative applications. This system will then be tested in experimental settings to validate its performance, accuracy, and reliability in differentiating between phantoms with different dielectric properties.

Future work will include upgrades to improve the probe's sensitivity and resolution, ensuring its reliability for real-world intraoperative applications. These advancements aim to further optimize the system, making it a valuable tool for enhancing surgical precision and improving patient outcomes. Additionally, while the proposed system relies on a VNA for signal measurement and analysis, its size, complexity, and cost can pose challenges for practical intraoperative applications. To address this, alternative detection circuits, such as compact spectrum analyzers or custom-designed integrated circuits, could be explored. These options offer potential for miniaturization and cost reduction while maintaining adequate performance for detecting variations in dielectric properties. Moreover, a stand-alone system specifically designed to meet the systems requirements is planned for development, ensuring a more practical and efficient solution for intraoperative use.

This initial study will open the way for precise real-time intraoperative measurements and potentially enhance surgical outcomes through real-time differentiation of tissue types resorting to mmWave technology.

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