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Towards real-time monitoring of microwave ablation using microwave-induced thermoacoustic signals

by

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Chapter 8

Chapter for the public

I am including this chapter to communicate my research to the general public, who has funded much of my work through programs like the National Science Foundation. The ultimate goal of my Ph.D. work has been the advancement of medicine using applied electromagnetics and acoustics. Providing accessible information and effectively communicating research to a non-expert audience is crucial for the ongoing public support of scientific advancement. I would like to thank the Wisconsin Initiative for Science Literacy (WISL) for enabling the communication of science to a broader audience.

8.1. Killing cancer with microwaves

You're probably already familiar with a common kitchen appliance that uses microwaves. Microwave ovens expose food to microwave energy. When the food absorbs microwave energy, it causes the food molecules to vibrate, which heats up the food. Microwave energy is a type of electromagnetic energy that is in the microwave frequency range. Much like food in a microwave oven, we can also use microwave energy to heat up and kill tumors. Microwave ablation (MWA) is a type of thermal therapy where a specialized antenna delivers microwave energy to diseased tissue. The diseased tissue absorbs the microwave energy and heats up, but the surrounding healthy tissue is unaffected. When biological tissue heats to temperatures beyond 60°C, or 140°F, the tissue dies.

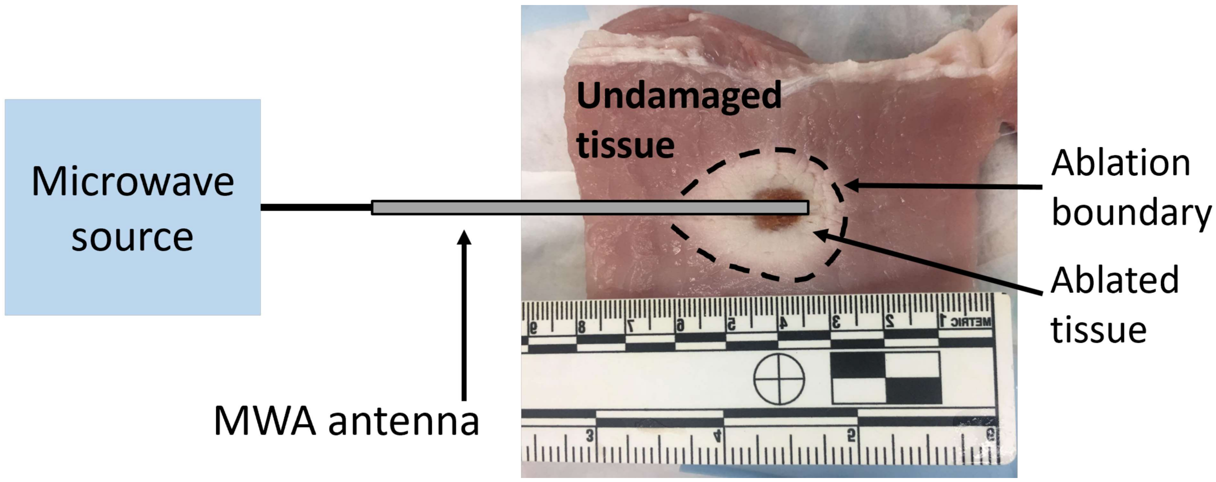

Figure 8.1: Microwave ablation using a minimally-invasive interstitial ablation antenna.

MWA treatments can be performed using a narrow diameter antenna that is inserted directly into the diseased tissue. After the diseased tissue is heated up and killed, the antenna is removed. Then, the human body can break down the dead tissue on its own.

MWA offers a lower risk, lower cost treatment option that has fewer side effects compared to conventional cancer treatments such as surgery. MWA can be a treatment option for cancer patients who may not be candidates for surgery. MWA is often used in conjunction with other conventional cancer treatments like chemotherapy. MWA is already used clinically to treat tumors in the liver, lung, prostate, kidney, bone, brain, and breast.

In order for MWA to be effective long term, clinicians need to confirm that the ablation zone, which is the area that has been heated and killed, totally includes the outer edges, or margins, of the tumor. One rule of thumb is that an ablation zone boundary should exceed at least one centimeter beyond the margins of the tumor — this rule of thumb reduces the chance of cancer recurrence. Right now, clinicians usually evaluate MWA procedures using ultrasound or X-rays. These two imaging methods are used to ensure that the antenna is positioned correctly before MWA and then after the procedure to confirm that the margins of the tumor have been fully ablated. However, neither ultrasound nor X-ray are good options for imaging MWA in real-time. MWA outcomes could improve if clinicians are able to watch what's happening during the procedure rather than

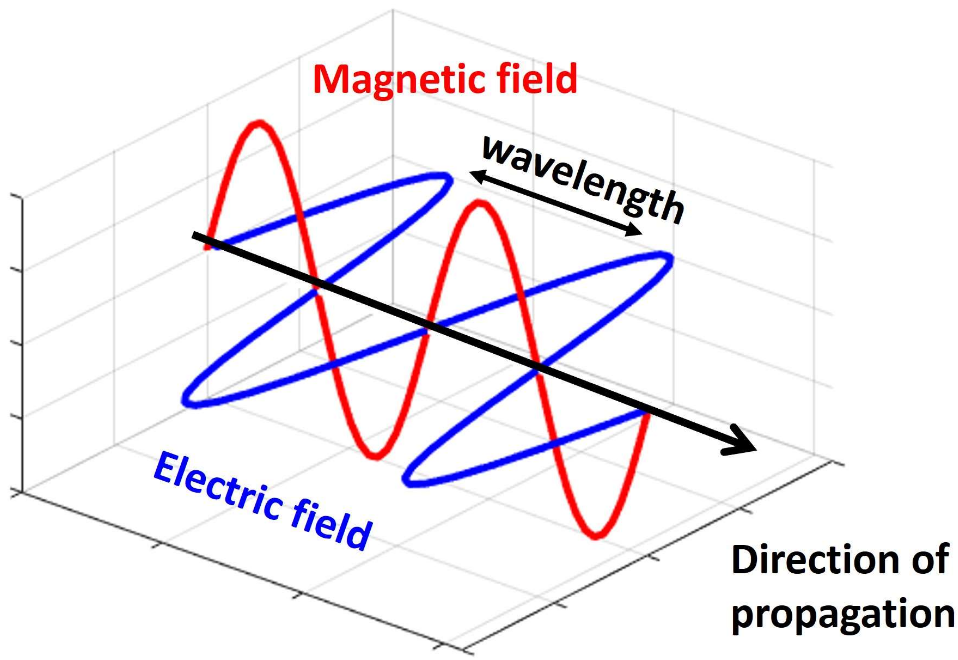

Figure 8.2: Electromagnetic wave propagation.

only being able to see before and after pictures. With reliable real-time imaging, we could do a better job confirming that the tumor is fully ablated.

8.2. Combining microwaves and acoustics

The crux of my research has been to develop a new way to monitor MWA in real-time using a combination of microwaves and acoustics. Just like microwaves are a type of electromagnetic energy, acoustic waves are a type of mechanical energy. Mechanical waves are the vibration of matter. Mechanical waves happen when molecules bump into each other, like a line of falling dominoes – each domino transfers its energy to the next in line. Electromagnetic waves and mechanical waves represent the propagation of different types of energy, but they can be described using very similar equations. Many people like to use a mechanical wave, such as a ripple propagating through water, as an analogy to describe electromagnetic waves.

Electromagnetic waves are the oscillation of electric and magnetic fields. An electric field is the region surrounding a charged particle. This region can exert force on other charged particles,

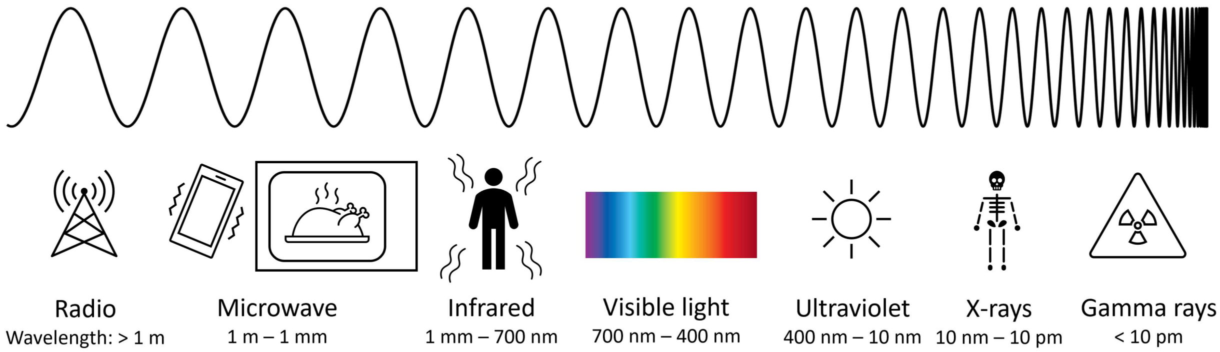

Figure 8.3: The electromagnetic wave spectrum. In addition to MWA and microwave ovens, microwave applications include Wi-Fi, Bluetooth, cell phone and satellite communications, weather radar, and radio astronomy.

by attracting or repelling. An electromagnetic wave is the synchronized oscillation of electric and magnetic fields that move through space, either in a vacuum or through a medium.

Microwaves refer to electromagnetic radiation that has wavelengths from one meter to one millimeter. Microwaves are particularly good at heating water. Water molecules, which are relatively small, are readily excited by microwaves compared to other frequencies of electromagnetic radiation. When microwave energy propagates through water, the water absorbs that energy, making the water molecules vibrate, which leads to a temperature rise. We take advantage of the convenient relationship between microwaves and water molecules with microwave ovens. Applying high power microwaves to food, which has a high-water content, causes the food to heat.

Microwave ovens are an example of a continuous-wave microwave source. Pulsed microwave energy has the potential to transform electromagnetic energy to mechanical energy. When pulsed microwave energy is absorbed by tissue, it causes the tissue's temperature to increase by a very small amount, usually less than a millicelcius. This small but fast temperature rise causes the tissue to expand. The volumetric expansion of tissue generates an acoustic wave, which propagates in all directions away from the source, and can be measured using an ultrasound transducer. Thus, electromagnetic energy is converted to mechanical energy. We call this type of problem multiphysics, meaning that there are multiple types of physics that need to be considered in order to understand

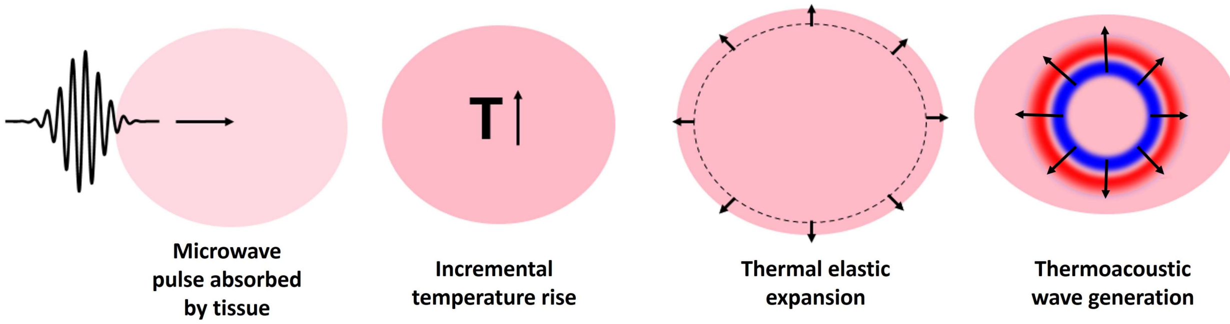

Figure 8.4: Microwave-induced thermoacoustic signal generation.

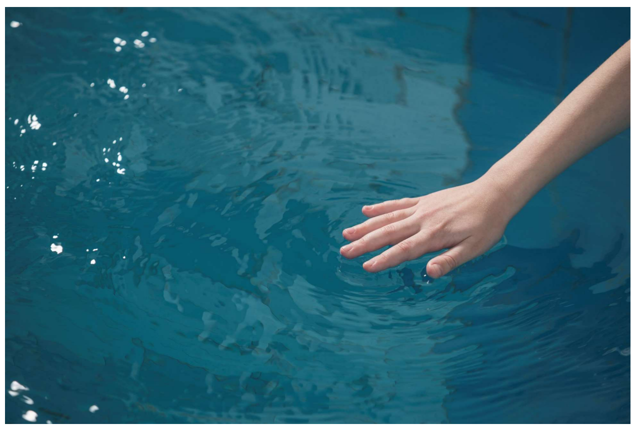

Figure 8.5: Slapping water can generate a ripple, similar to how pulsed microwave energy can generate an acoustic wave. (Microsoft stock image)

what's going on. In this case, we consider electromagnetics, heat transfer, and acoustics.

Using the water ripple analogy, exposing tissue to continuous wave microwave energy is like gently placing your hand in water. Exposing tissue to pulsed microwave energy is like repeatedly slapping the water. Each slap (like each electromagnetic pulse), will generate a ripple in the water, i.e. a mechanical wave.

The mechanical wave generated by a microwave pulse is called a thermoacoustic (TA) wave. When we detect one of these waves, we refer to it as a signal. TA signals can tell us important information about the medium that they were generated in and the medium that they propagated through. We can track characteristics of TA signals, such as amplitude (in other words, the strength of the signal), energy, or time of arrival, during a MWA procedure. TA signal characteristics

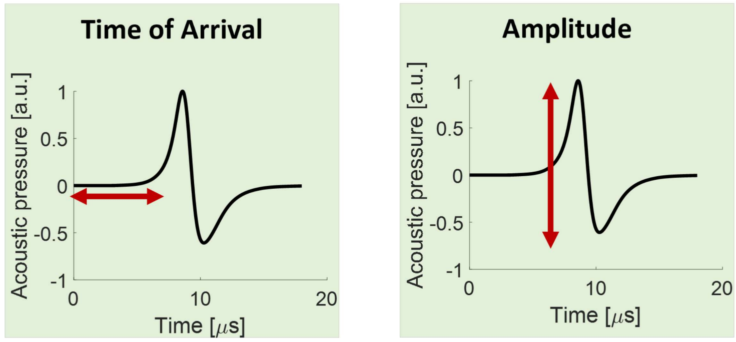

Figure 8.6: TA characteristics like the time of arrival and amplitude will change as temperature rises.

depend on the material properties of the medium, including the dielectric (the dielectric properties of tissue tells us how the tissue reacts to electromagnetic energy), thermal, and acoustic properties. All these properties are temperature-dependent, meaning that they change as temperature changes. TA signal characteristics measured on the surface of tissue can give us clues as to what's going on inside the ablation zone.

8.3. My research

My Ph.D. research has been centered on investigating the feasibility of using microwave-induced TA signals to monitor MWA in real-time. In my proposed therapy-imaging setup, the MWA antenna is used for two simultaneous purposes: perform MWA, and generate TA signals. Conventional microwave-induced TA imaging systems use an external microwave antenna to radiate the tissue uniformly in order to generate TA signals. Existing TA systems aren't designed to image tissue that's actively being heated; most are designed for diagnostic purposes only. In contrast, my TA system uses an internal antenna to radiate the tissue just around the part we want to heat up, i.e. the tumor, and this system must be designed in the context of MWA, so we must consider how temperature will impact TA signals.

Before we can use TA signals generated from a MWA antenna to create images of MWA zones during a procedure, there's a lot of intermediate steps to address. My work has focused on inves-

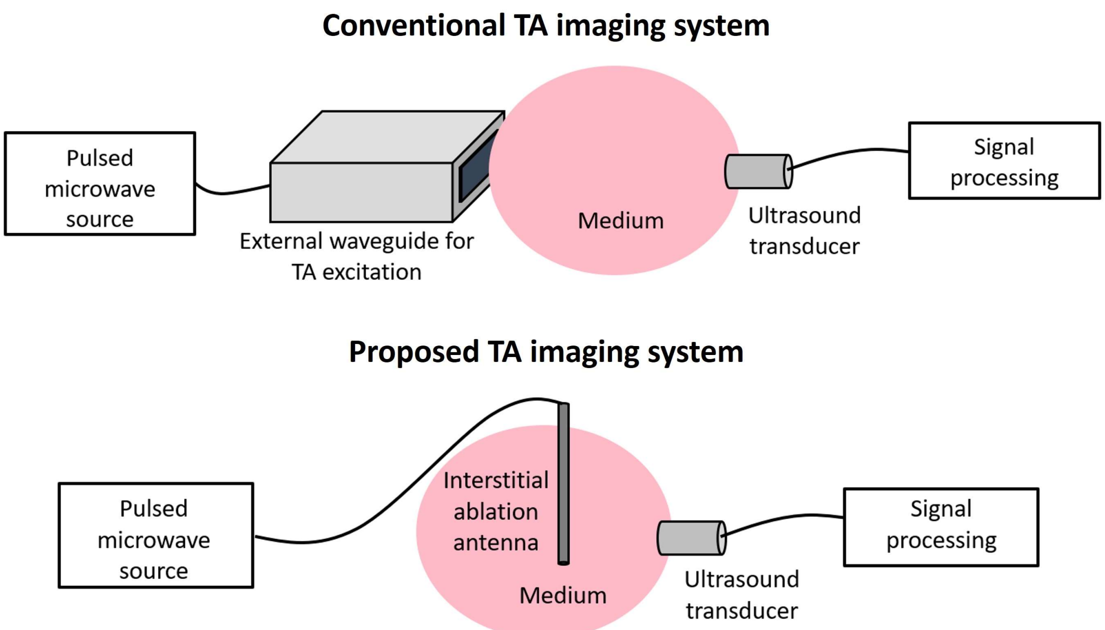

Figure 8.7: Conventional TA imaging systems use an external microwave waveguide to uniformly radiate the tissue to generate TA signals. We propose using an internal microwave antenna to use nonuniform radiation to simultaneously ablate the tissue and generate TA signals.

tigating these intermediate steps, which are all necessary prerequisites to the ultimate objective of using TA signals to image MWA. In the rest of this chapter, I will break up my research into two parts: modeling and experiments. For the modeling section, I will summarize the multiphysics simulation model that I developed to better understand the fundamental mechanisms of TA generation and propagation. In the experimental section, I designed an experimental system to measure TA signals during MWA and I investigated new ways to track the evolution of TA signals.

8.4. Modeling microwave-induced thermoacoustic signals

I developed a multiphysics simulation model that calculates the generation and propagation of TA signals during MWA. A numerical simulation is a way to solve the equations that describe a physical phenomena by breaking up the simulation domain into tiny parts. The simulation domain is the region that you plan to study – for example, I want to study the antenna and the region of tissue immediately surrounding the antenna. My model is a numerical simulation that incorporates electromagnetics, heat transfer, and acoustics physics. I set up a domain that contains the components of a MWA scenario: a MWA antenna and a surrounding biological tissue medium (see Fig 8.9. The dielectric, thermal, and acoustic material properties of the domain were set to match the different materials in the domain. In this case, the antenna is made out of copper and Teflon, and the surrounding medium is water. The domain is two-dimensional axisymmetric because the antenna is symmetric along its center axis. A 2D simulation domain uses less computer resources compared to a 3D domain, and therefore, it takes less time to run on my computer.

The simulation model is made up of two processes: a coupled electromagnetic and heat transfer physics to simulate MWA, and an acoustics physics to simulate TA signal generation. The first process begins with the electromagnetic simulation, which calculates the specific absorption rate (SAR). SAR tells us where microwave energy is absorbed when the antenna is powered by a microwave source. Then, the SAR results are sent to the heat transfer simulation, which calculates the temperature rise that results from microwave absorption. The material properties are temperature-dependent, meaning that they change as microwave heating occurs, creating a cyclical

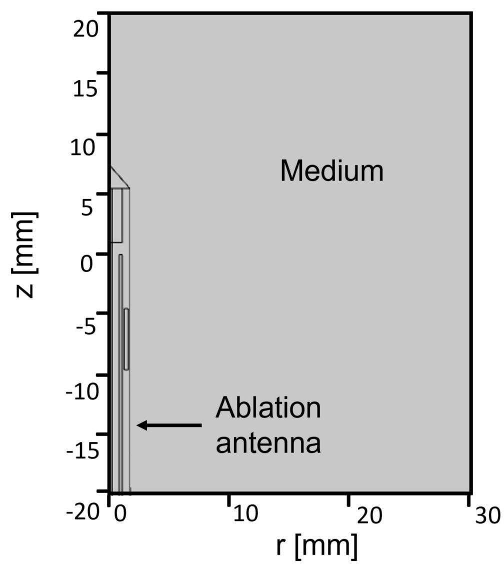

Figure 8.8: The 2D axi-symmetric simulation domain.

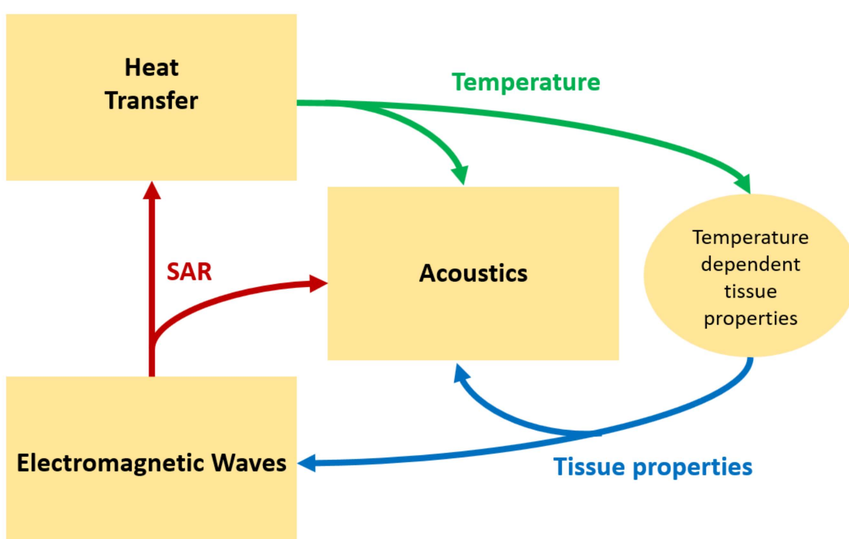

Figure 8.9: The multiphysics modeling technique to incorporate electromagnetics, heat transfer, and acoustics physics.

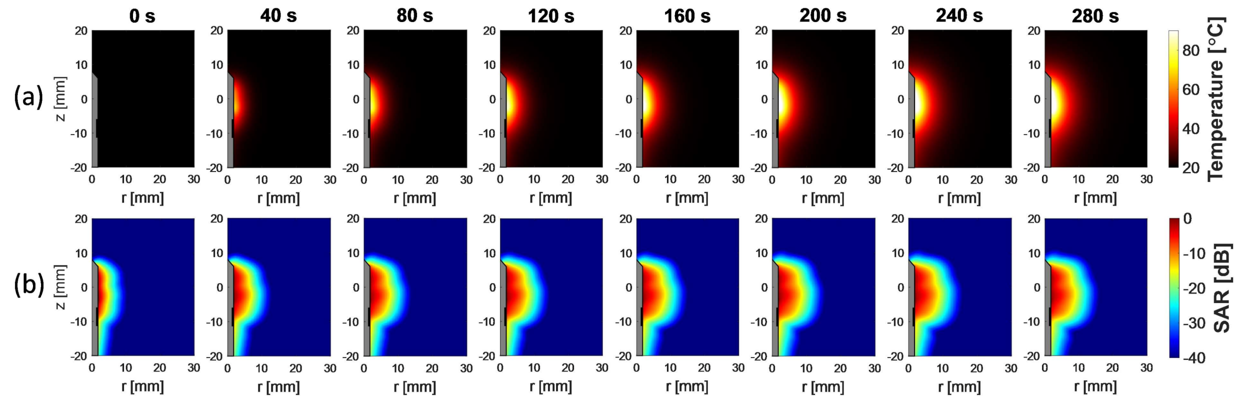

Figure 8.10: Results from the first process. Temperature (top row) and the corresponding SAR (bottom row) as a function of time throughout the course of MWA. As the temperature rises, the SAR becomes more dispersed because the dielectric properties are temperature-dependent.

process. The SAR is calculated $\rightarrow$ temperature rise $\rightarrow$ update material properties $\rightarrow$ update SAR, and repeat. The first process gives us the SAR and the temperature throughout the course of a MWA procedure.

The second process, the acoustic process, takes the SAR and the temperature and uses it to calculate a TA signal that is generated from one microwave pulse. The first process that calculates MWA operates on a timescale that is on the order of seconds. The second process is on the order of microseconds. At any snapshot in time within the first process, I can take the SAR and the temperature and input it to the acoustic process, which calculates the TA signal generation from one microsecond microwave pulse. For example, if I want to know what a TA signal will look like 100 seconds into a MWA, I will pause the first process at 100 seconds, and then run the acoustic process from 100 seconds to 100 seconds plus 20 microseconds.

8.4.1. Take away

The simulation model is a tool to investigate TA signals in a controlled environment. I used this tool to test how different parameters impact TA signal characteristics, like the amplitude or the time of arrival. For example, the results shown in Fig. 8.12 show us that TA signals change significantly

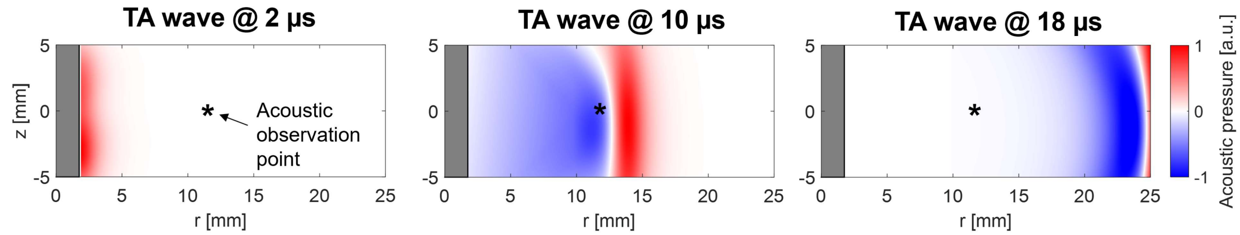

Figure 8.11: Results from the second process. The TA signal propagates away from the antenna. The red corresponds to the positive part of the TA wave and the blue corresponds to the negative part of the TA wave.

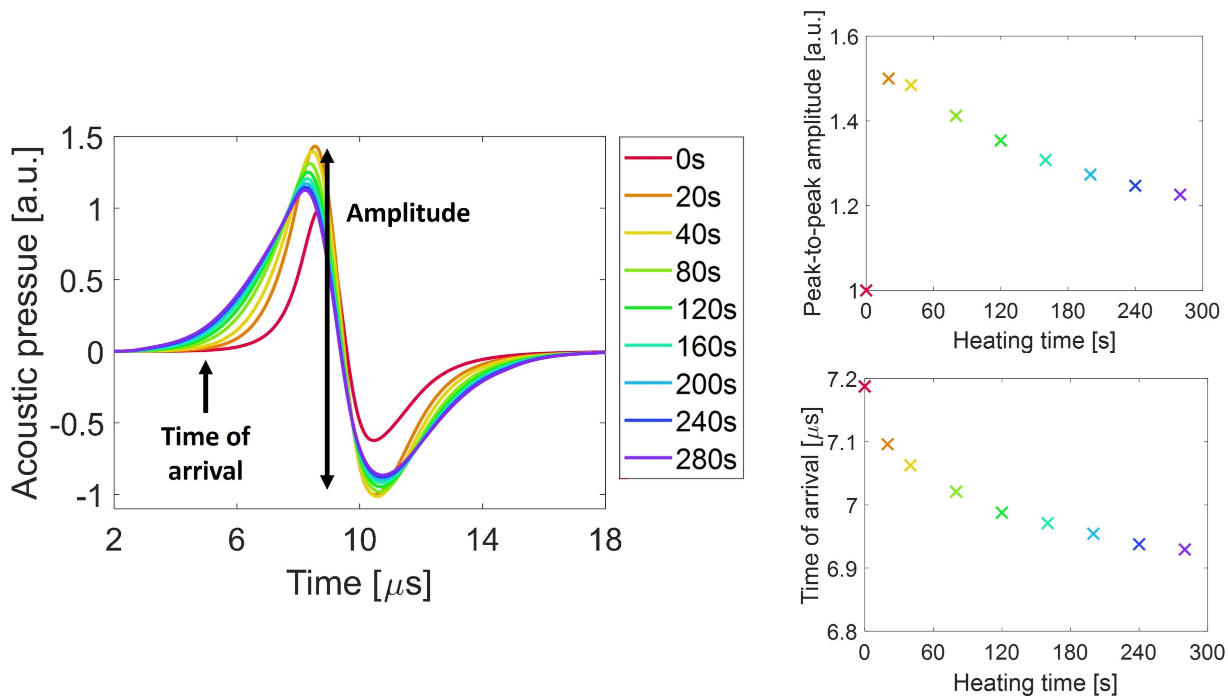

Figure 8.12: Results from the second process. The TA signal detected at the acoustic observation point. We can track TA characteristics such as the peak-to-peak amplitude and the time of arrival throughout the course of MWA.

during MWA. Both the amplitude and the time of arrival of the signal decrease throughout the course of MWA. Therefore, TA signals contain information about the ablation zone, telling us that these signals can be used to ultimately create an image of the region in which the signals are generated.

Simulation models can only get you so far. The accuracy of a model is tied to the accuracy of the material properties that are used by the model. If the material properties are unknown, then the model can't accurately predict TA signal characteristics. For example, some temperature-dependent material properties of biological tissues are currently not known, such as the coefficient of thermal expansion (CTE). The CTE tells us how much a material expands due to temperature rise. The higher the CTE, the more the tissue will expand, and the TA signal amplitude will be larger. Going back to my water slapping analogy, if I slap water and wet cement with the same force, the water will ripple more than the cement; therefore, the CTE of water would be higher than the CTE of cement. Measuring the CTE of a material at room temperature is difficult and requires specialized equipment. Measuring the CTE as a function of temperature is even harder, which is likely why it hasn't been reported in literature.

8.5. Measuring microwave-induced thermoacoustic signals

The second aim of my Ph.D. work was to experimentally measure TA signals. I designed an experimental system that measures TA signals generated during MWA in liver tissue. Then, I used the measured TA signals to investigate how TA signal characteristics change as a result of MWA. The results from this work established the prerequisites for using TA signals to monitor MWA in real-time. I chose to perform the experiments using cow livers because they're similar in material properties to human livers. Cow livers are also very large and homogeneous – they're easy to section into smaller pieces without major veins or arteries.

Fig. 8.13 shows the experimental setup for measured TA signals during MWA. I obtained fresh cow livers from a local butcher and sliced them into 20 x 20 x 20 cm sections. For each experiment, I inserted a MWA antenna into an unused liver section and positioned an ultrasound transducer to

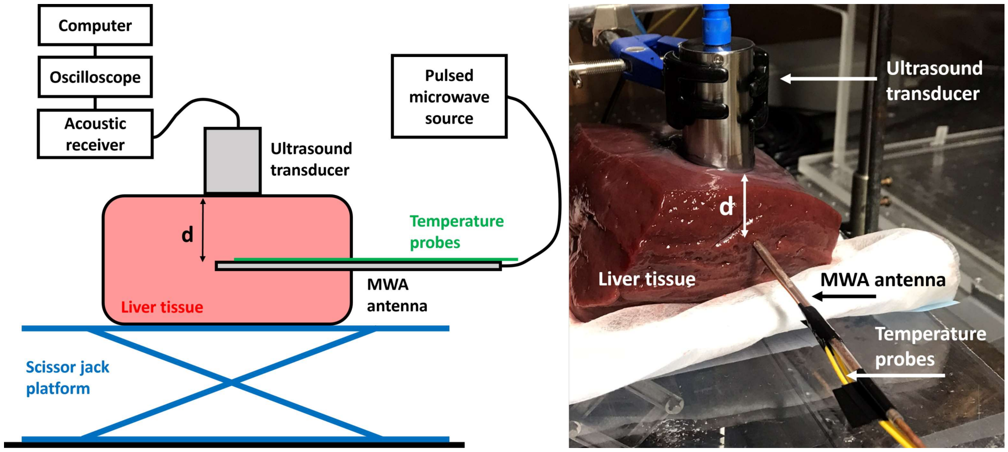

Figure 8.13: The experimental setup for measuring TA signals in liver tissue during microwave ablation.

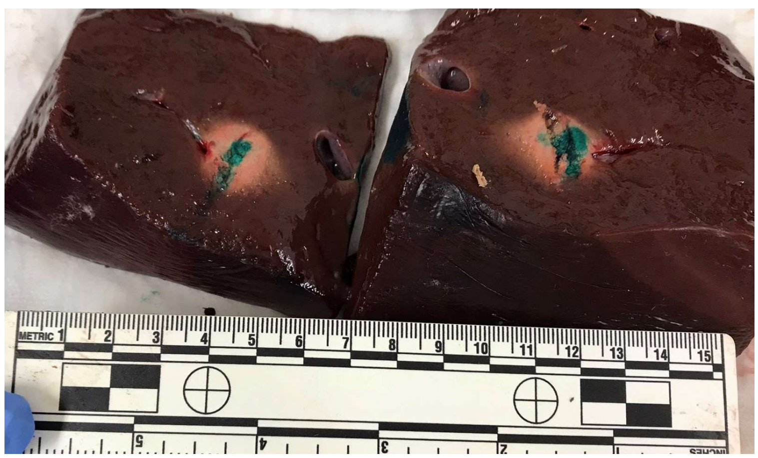

Figure 8.14: The two halves of a sliced section of liver after MWA.

point at the antenna. The antenna had a temperature probe taped to its tip to measure the internal temperature during MWA. I turned on the microwave source and let the liver tissue heat up while measuring TA signals every one second.

After each experiment, I sliced open the liver section along the path of the antenna, and recorded the dimensions of the ablation zone. Fig. 8.14 shows a representative liver section after it has been sliced. The path of the antenna is marked in green ink and there is an ablation zone (light pink tissue) around where the tip of the antenna was positioned. I repeated this procedure 20 times each for two average microwave powers, 5 watts and 10 watts.

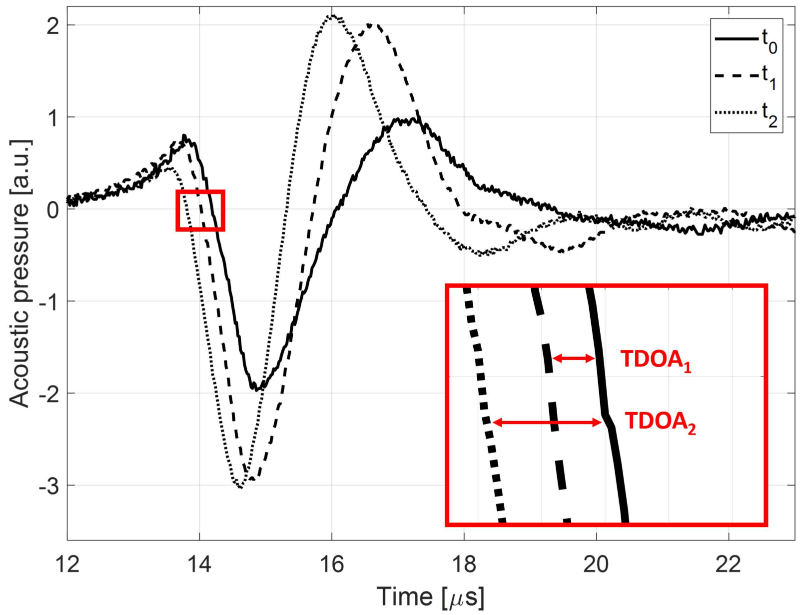

Figure 8.15: A TA signal measured at three different times during MWA in liver: t_0 = 1 s, t_1 = 100 s, and t_2 = 300 s.

Using the data from these experiments, I focused on two TA signal characteristics: time difference of arrival (TDOA) and energy. TDOA is the time of arrival of a TA signal relative to the first signal measured. I can slap my water and measure the time it takes for the ripple to reach an observation point, and compare that time to another slap later on in the process. In this case, the reference signal is the first TA signal measured at time = 1 second. Fig. 8.15 shows representative TA signals measured at 1 s, 100 s, and 300 s during a MWA ablation procedure. The TA signal arrives earlier and earlier in time during MWA, and thus the TDOA is negative and becomes larger in magnitude. The amplitude of the signal becomes larger during MWA, and thus the energy of the signal increases. It's not easy to understand why we see these changes with just three TA signals, so I tracked the TDOA and the energy of every single TA signal I measured and combined it into the next figure.

The median values of TDOA and energy are plotted in Fig. 8.16 for the two microwave powers. The error bars represent the 25th and 75th percentiles of the data, which helps visualize the variability of TDOA and energy across all the experiments. The TDOA decreases throughout the

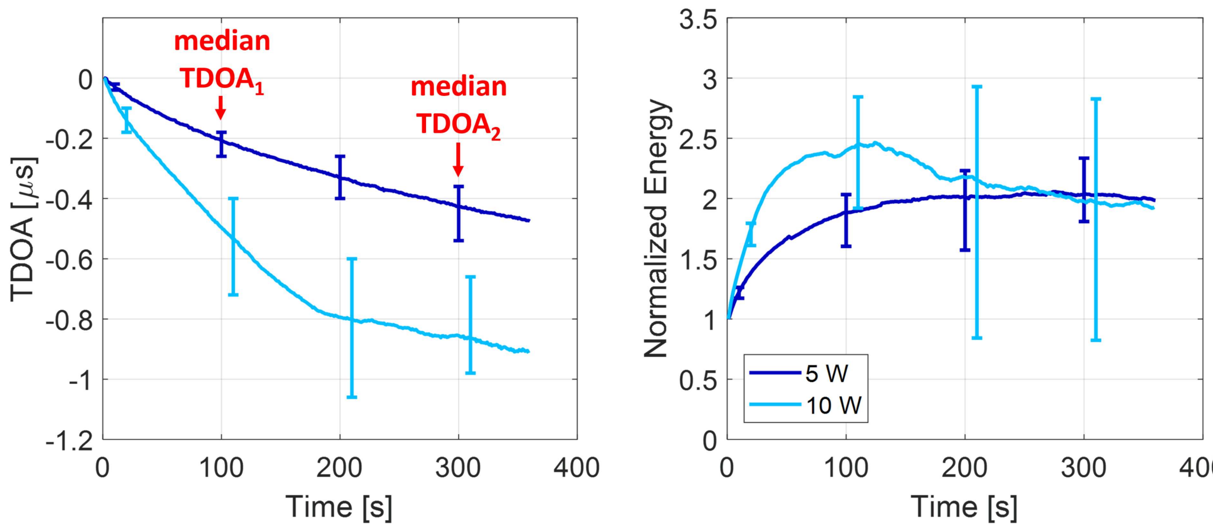

Figure 8.16: The median TA signal characteristics during MWA. The TDOA decreases, i.e. TA signals arrive earlier in time relative to t = 0 seconds. The TA signal energy increases during MWA.

course of MWA, meaning the signals arrive earlier and earlier. We see this because of two main reasons: the speed of sound in liver tissue increases as temperature increases, and also because the tissue shrinks during MWA, which causes the signal to arrive earlier due to the distance between the antenna and the ultrasound transducer decreasing.

The energy of the TA signal generally increases as a function of time, meaning the amplitude of the TA signal gets larger and larger throughout the course of MWA. The increase in energy could be because the CTE of liver increases as temperature increases. However, there is more variability in the energy of the signal compared to the TDOA of the signal. More variability makes energy a less reliable TA characteristic to track.

8.5.1. Take away

Liver tissue undergoes permanent physiological changes when it's heated to temperatures beyond 50°C: coagulation, aka cooking, causes protein denaturation (when the tissue proteins permanently change shape), water loss, and tissue shrinkage. These tissue changes will change dielectric, thermal, and acoustic properties, all of which impact TA signal characteristics. In these

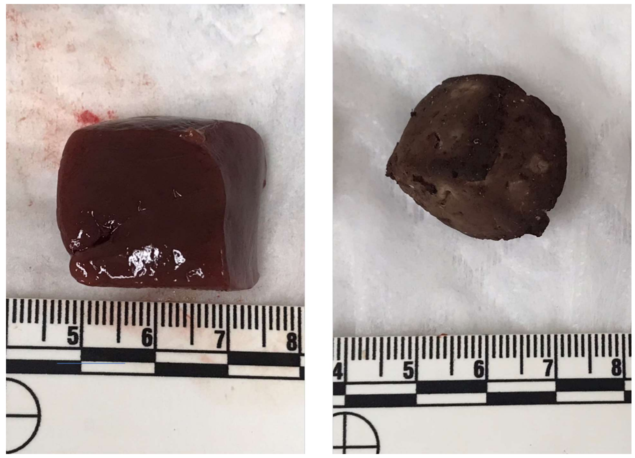

Figure 8.17: Liver tissue shrinks when it is cooked. A 1 cm x 1 cm x 1 cm cube of fresh liver (left) and the same cube of liver (right) after it's boiled in water for 1 hour. Tissue undergoes a similar transformation when ablated. These changes will impact TA signals that are being generated in liver tissue.

experiments, the internal temperature reaches up to 50°C for the 5 W experiments and as high as 70 °C for the 10 W experiments.

Our results show that as the MWA antenna heats up tissue, TA signal characteristics change significantly. This is a good sign – it means that TA signals contain information about the MWA zone. The information that TA signals carry may be used to monitor MWA, and eventually image MWA, in real time.

8.6. Conclusion

The dominant finding from my work is that TA signals contain information about the region in which they were generated, and thus TA signals generated during MWA may be able to tell us about what's happening in an ablation zone. Imaging MWA in real-time will help interventional radiologists and clinicians improve the outcomes of MWA: mainly, reduce the risk of cancer recurrence by ensuring that the tumor has been completely killed by MWA while minimizing damage to healthy tissue. After completing my PhD, I will join the Los Alamos National Laboratory as a research scientist. I'm excited to apply my expertise in a specific area of microwave applications to a much broader field of applied electromagnetics and acoustics.