



# Thermal Ablation Interventions for the Treatment of Localized Tumors: The Development of a Software-Prototype for Supporting the Planning Phase on Basis of Patient Specific Anatomy

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# Abstract

## Background and Goal

Thermal ablation as a complementary treatment for localized tumors has been proving oneself for the last years and is applied more and more frequently. Different techniques (e.g. Radiofrequency ablation, Cryoablation etc.) are used to destroy cancer tissue either by heating or freezing. The treatment is applied in a minimal-invasive manner in contrast to surgical resection. Medical imaging modalities, such as Magnetic resonance imaging, computed tomography and ultrasound are essential for this treatment form. Although thermal ablation is particularly used for the treatment of small tumors worldwide, metastases still re-appear more frequently than in case of surgical resection. The successful treatment outcome depends on many factors. Despite of the additional removal of a 1cm margin around the tumor, metastases still re-occur oftentimes. Incomplete removal of the tumor is mostly the reason for this circumstance.

The collaboration of different experts and techniques suggest, that the operators benefits from a software-platform for supporting the operators during the planning-phase. The software enables the abstract simulation of the intervention on basis of the patient specific anatomy. Multiple applicators can be placed into the virtual body and the resulting ablation zone will be visualized on basis of data of the respective device vendors. The operators are enabled to see which structures lie in the trajectory of the applicator and above all which anatomical structure are adjacent to the tumor. Large vessels adjacent to the tumor will most likely limit the dimension of the ablation zone caused by the blood flow. Those and other effects will be detected and avoided by applying the planning-software.

## Methods and Results

Before developing the prototype the processes of the thermal ablation intervention must be understood. Different ablation techniques are described in this thesis. Devices of different vendors were evaluated to determine the different ablation zone shapes. The requirements on such a planning-system

base upon the research work of Dr. Wolfgang Schramm.

The software was developed as a module-extension of the Slicer software framework. The modular structure of Slicer allows the extension of its own functionality by adding different module types. In the process a Python scripted module was developed to implement the functionality of such a planning-software as a prototype. The resulting software is open source and free to access at <https://github.com/HaichaoMiao/Slicer4-Module>.

# Zusammenfassung

## Hintergrund und Ziele

Thermische Ablation als eine komplementäre Behandlung für lokale Tumore hat sich seit Jahren bewährt und wird immer häufiger eingesetzt. Dabei werden unterschiedliche Techniken (wie Hochfrequenzablation, Kryoablation etc.) eingesetzt um das Krebsgewebe entweder durch Erhitzung oder Erfrierung zu zerstören. Die Behandlung erfolgt minimal-invasiv im Gegensatz zum chirurgischen Eingriff, wobei bildgebende Verfahren wie Magnetresonanztomographie, Computertomographie und Ultraschall unverzichtbar sind.

Obwohl thermische Ablation vor allem für die Behandlung von kleineren Tumoren immer häufiger eingesetzt wird, ist jedoch das Wiederauftreten von Metastasen häufiger als bei der chirurgischen Resektion. Der Erfolg von thermischer Ablation ist von vielen Faktoren abhängig. Trotz der zusätzlichen Entfernung eines 1cm Abstandes um den Tumor, kommt es häufig zu Wiederauftreten von Metastasen. Eine unvollständige Entfernung ist oft der Ursache dafür.

Die Multidisziplinarität dieser Behandlung erfordert den Einsatz mehrere Experten bzw. Techniken. Es ist daher naheliegend eine Software-Plattform zu entwickeln, die die Operatoren vor allem während der Planungs-Phase unterstützt. Die Software ermöglicht abstrakte Simulation des Vorganges aufgrund der patientenspezifischen Anatomie. Mehrere Applikatoren können in den virtuellen Körper eingebracht und die resultierenden Ablationszonen aufgrund der Angaben des Geräteherstellers visualisiert werden. Die Operatoren haben dadurch die Möglichkeit zu erkennen, welche Strukturen in der Einstichsbahn des Applikators liegen und vor allem welche anatomische Strukturen am Tumor anliegen. Insbesondere große Gefäße nahe am Tumor können das Ausmaß der Ablationszone beschränken, da diese die thermische Energie ableiten. Diese und andere Effekte können im voraus erkannt und vermieden werden mit der Planungssoftware.

## Methoden und Ergebnisse

Für die Entwicklung des Prototyps musste zuerst der Vorgang der thermischen Ablation verstanden werden. Unterschiedliche Ablationstechniken wurden abgebildet und beschrieben. Geräte unterschiedlicher Hersteller wurden ausgewertet um die unterschiedlichen Formen der Ablationszone zu bestimmen. Die Anforderung an ein solches Planungssystem basiert insbesondere auf die Vorarbeiten von Dr. Wolfgang Schramm.

Die Software wurde als Modul-Erweiterung des Slicer Software-Frameworks realisiert. Der modulare Aufbau von Slicer erlaubt die Erweiterung seiner eigenen Funktionalität mit unterschiedlichen Modultypen. Dabei wurde ein "Python scripted" Modul entwickelt um die Funktionalität einer solchen Planungs-Software als Prototyp zu implementieren. Die fertige entwickelte Software ist open source und auf <https://github.com/HaichaoMiao/Slicer4-Module> frei zugänglich.

# Introduction

Thermal Ablation as a treatment for localized tumors has been established continuously over the past years. Malignant liver tumors are one of the most common forms of cancer in the world, but unfortunately chemo and radiation therapy are ineffective against liver tumors [ea00]. Due to the fact, that many patients are no surgical candidates, thermal ablation techniques provide complementary treatment to eliminate or shrink tumors in a minimal invasive way and promises significant lower risk of major complications. There is numerous literature that describes the use of thermal ablation for nearly all cancer types.

Medical imaging modalities have enabled the use of thermal energy to kill tumors without surgically cut the patient open. In the literature, these thermal ablation interventions are categorized as minimal invasive techniques. The interconnection between medical practice and technology has become tighter, as advances in technology are made. The intervention is therefore oftentimes not performed by one physician, but by a collaboration of several specialists. They are often referred as operators<sup>1</sup>. The complex procedure of thermal ablation and the necessity of collaboration suggest that many benefits can be drawn from a planning-software, that enables outcome simulation on basis of the patient's specific anatomy.

The development of a planning-software needs both, knowledge of the thermal ablation techniques and different software technologies. The architectural design of the planning-software will built upon software libraries and frameworks of third parties. These software technologies must be studied in detail. Accordingly, one major part of this thesis concentrates on the development process of the planning-software.

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<sup>1</sup>see [ea04]



# Chapter 1

## Image-guided Thermal Ablation Techniques

### 1.1 Introduction

#### 1.1.1 Overview

Different ablation methods are used in clinical environment. The decision which method is going to be used, not only depends on the tumor location, but also on the geographical region where it comes to use. This chapter compares the different thermal ablative techniques in tumor therapy that are commonly used.

Although the rapid advancement in ablative techniques has taken place within the past 20 years, experiments with ablation of tissues using radiofrequency (RF) has been already documented at the end of the 19th century [FGC05].

What all ablative techniques in general have in common is, they attempt to kill every viable malignant cell within the designated area using thermal energy sources in a minimally invasive manner. At the same time minimal damage to the surrounding organs is done. There are several ways to accomplish this, but they can generally be divided into two groups, based on whether heating or freezing is utilized to kill tumor cells [AG05]. Currently the most common method is Radiofrequency Ablation, but other techniques are coming more and more to use. Cryoablation is used effectively in the treatment of prostate and kidney cancer. Microwave Ablation (MWA) is widely used in the Asian region. Especially Microwave Ablation has shown high potential in treating pulmonary tumors due to the significant larger ablation zone compared with RF [ea09].

Other thermal energy sources are Laser and High-intensity Focused Ultrasound.

Chemical substances can also be used to kill tumor cells. Chemical Ablation

tion was documented being efficient in destroying hepatocellular carcinoma (HCC). Thereby chemical ablative substances (e.g. ethanol or acetic acid) are injected into the tumor [AG05]. These techniques will not be in the main focus of this thesis.

### 1.1.2 Image Guidance and Minimal Invasiveness

The ablation of tumor with thermal energy sources (in literature also referred as tumor ablation) represents the non-surgical alternative solution for patients with cancer. Especially with the rapidly increasing advancement in imaging technologies, the techniques became lesser invasive. Even during an intraoperative procedure imaging techniques, such as intraoperative ultrasound, are necessary. Hence imaging is essential during the ablation process, since the interventional radiologist utilizes it to target the tumor inside the patients body. Depending on the imaging modality and tumor properties, surgery is often not required.

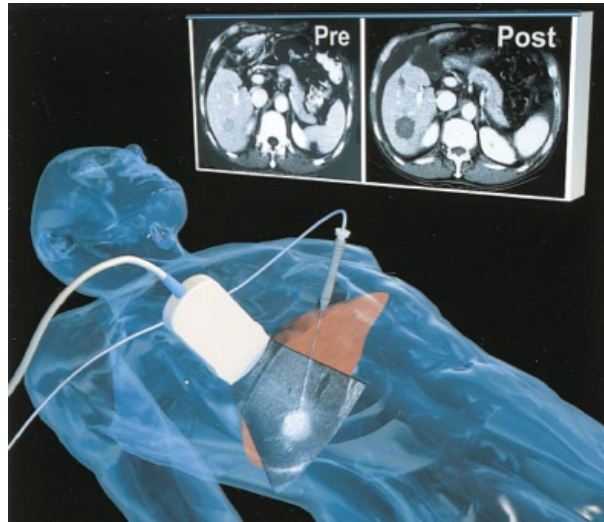


Figure 1.1: Tumor ablation intervention under Ultrasound-guidance with CT scans of the patient before and after the ablation. Image taken from [ea00]

### 1.1.3 Benefits of Thermal Ablation

The increasing application of thermal ablation demonstrates the benefits from thermal ablation.

- Minimal invasiveness. Small probes are punctuated through the skin into the center of the tumor (percutaneous). Due to imaging technologies, there is no need to cut through the skin in most cases.

- Compared to surgery, there are less complications reported during and after the procedure.
- Re-treatment possible. This is especially relevant when metastases reappear.
- Less tissue is removed compared to surgical resection, because only the tumor and a safety margin of 1cm have to be ablated.
- Alternative to surgery. Patients who are not surgical candidates or patients with few small Tumors are qualified for thermal ablation.

## 1.2 Overview: Thermal Ablation Techniques

Thermal ablative techniques differ mainly by their method of generating heat or cold.

### 1.2.1 Radiofrequency Ablation

Since the early 1990 there has been enormous development of percutaneous Radiofrequency technology [Hel08]. RFA as a treatment for primary and secondary hepatic malignancies has been performed successfully for more than 10 years. But there has also been reports for RFA treatment for nearly all kinds of tumors.

#### Technique of Radiofrequency Ablation

In RFA high-frequency alternating current (typically between 450 - 500 kHz) is applied through an electrode into the biological tissue. Thereby an electric field within the tissue is established which oscillates with the applied radio frequency inducing ionic friction. When enough energy is deployed over a certain amount of time, the ionic friction results in loss of heat energy, which emerges into the tissue by the phenomena of convection. A coagulative necrosis follows.

The efficacy of the RFA and the resulting size of the coagulation zone depends on the following factors [Hel08]:

- amount of energy deployed
- duration of exposure
- electrode design
- tissue-specific factors (heat conductivity and conversion)
- "heat sink" and "oven effect"

## Electrodes

As mentioned before, the RF current is deployed through an electrode directly into the tissue. In general these electrodes consists of an isolated shaft and an active tip. Various electrodes creates different coagulation volume shapes, mostly between 2 and 5 cm in diameter.

## Radiofrequency Generators

The ablation process is controlled over the generator. Concerning the above mentioned tissue-specific and other factors, the amount and duration of energy exposure has to be well adapted for the tumor. The process is thereby very device-dependent. Thus the personal experience of the operator is essential to ensure efficient treatment of the disease [ea04].

## Procedure

RFA is usually performed under conscious sedation. Ultrasound (US), computed tomography (CT) and magnetic resonance imaging (MRI) are normally used for targeting the probe into the tumor and monitoring the result. It usually takes more than one placement, especially when several tumors has to be targeted.

These imaging methods has both advantages and disadvantages. US is the most used worldwide, because with this setting no radiologist is required for the procedure. CT is the most used imaging modality by interventional radiologist [Hel08]. It has anatomically exact imaging and is widely available. Though MRI guidance has high contrast tumor-to-tissue, it has the necessity for MR-compatible equipment [Sch10]. This circumstance does not exclude MRI, but it is often the reason for using other imaging modalities.

RFA is perceived by some clinicians as a simple treatment form, where simply just by inserting a needle and "cooking" the tumor [ea04]. As showed above, the procedure is more complex and the efficacy of the treatment is dependent on many factors.

## Conculusion

Studies has shown Radiofrequency Ablation to be an effective, safe and low-risk technique for treating liver tumors. It has come more and more to use over the past years.

RFA is a technology-based treatment form and efficient application is thereby highly dependent on the experience of the operator. Due to the treatment's interdependence on various factors and its highly conjunction with technology, it can be assumed that a planning phase is necessary.

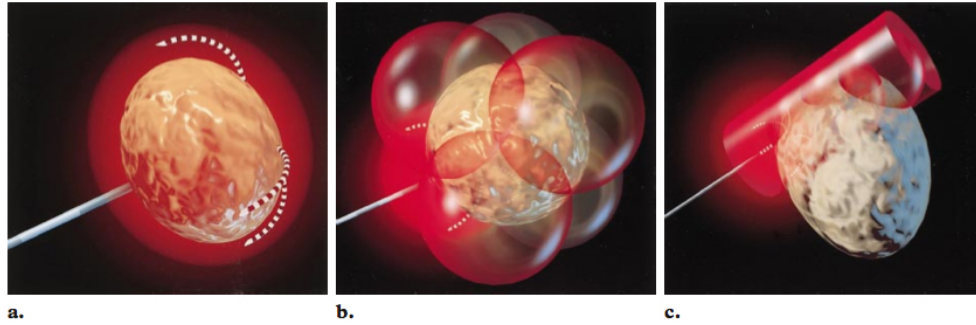


Figure 1.2: The figures show the spherical thermal injuries done by the different RFA treatment strategies. Tumors less than 2cm can be treated with a single ablation, larger tumors in size need to be performed multiple times [ea00]. Images taken from [ea00]

### 1.2.2 Cryoablation

The destruction of tissue by freezing is one of the oldest methods of tissue destruction known to mankind [ea05a]. But substantial progress in destroying cancer tissue has been made not until recently. In the 60s, nitrogen-cooled probes for cryotherapy established in hepatic surgery. Probes were relatively large in size and open surgical was necessary for the placement of the probe [ea10]. The development of smaller percutaneous cryoprobes, using argon gas eliminated the risks associated with open surgery [AG05]. Currently Cryoablation (CA) is been successfully used to treat several types of tumor.

The major advantage of CA is the clear visualization of the iceball generation under different imaging modalities. This ensures precise monitoring and therefore better control of the ablation zone dimension.

#### Technique of Cryoablation

In order to treat effectively and have control over the process the operator has to understand the mechanisms of cryogenic injury. In recent years freezing has not only used to destroy tissue, but also to preserve. The cell destruction with freezing is achieved by two major mechanisms. Cells are injured by ice crystal formation and the microcirculatory failure, which occurs in the thawing period [GB98]. At low freezing rates, the freezing propagates through the extra-cellular space, which causes water to be drawn from the cell and cell results in osmotic dehydration [AG05]. At faster freezing rates, intra-cellular ice crystal formation causes lethal damages to organelles and membrane [AG05].

## Devices

As mentioned before, the development of argon-based systems replaced liquid nitrogen units, because argon has major advantages to nitrogen. As an example, Argon-based systems circulate very fast and as a result, iceball formation emerge very quickly. Probe tips of these systems reach temperatures around  $-150^{\circ}\text{C}$ .

The two Cryoablation systems available in the United States are CRYOcare (EndoCare inc., Irvine, California) and CryoHit (Galil Medical Ltd., Wallingford, CT) [WJ05]. The latter is the only unit with MRI compatible cryoprobes [cry]. They are both argon-based and use simultaneously multiple probes for the placement in the shape of the tumor in order to cover it.

## Probes

Both of above mentioned systems use eight sharp-tipped cryoprobes, that can directly place into the tumor. CRYOcare uses 2.4-4.9mm OD probes and CryoHit 1.4-3.4mm probes.

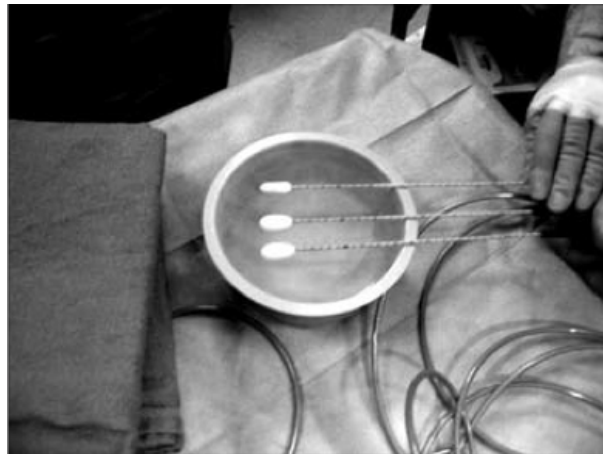


Figure 1.3: The picture shows the ellipsoidal ice ball formation around the probe tip (Galil Medical, Yorkneam, Israel). Picture taken from [ea10].

### 1.2.3 Microwave Ablation

Microwave Ablation (MWA), the latest development in tumor ablation, has been shown to have potential advantages over RFA, which is the most extensively applied modality. Zones of ablation are significantly larger and therefore faster treatment time can be achieved, compared to RFA. Yet, there is no approved device for patient treatment within the USA or Eu-

rope but in the Asian region devices has been developed since the early 90s [BDP08].

### Technique of Microwave Ablation

In Microwave Ablation tissue heating and resulting cell death is induced by high-frequency electromagnetic waves in the GHz order. Microwaves has wavelengths between infrared light and radio waves. Similar to RFA, a microwave antenna is placed into the tumor and emits electromagnetic microwaves into the surrounding tissue. It causes water molecules with an electric dipole moment to align themselves to the alternating electric field induced by microwaves. These oscillations of water molecules inside the cells results in warming. Macromolecules are not effected by microwaves but they are heated by convection nonetheless resulting in coagulation necrosis.

Although water molecules has a resonance frequency of ca. 22,2 GHz, they typically absorb 50%-60% of electromagnetic energy effectively in the range of 1-2 GHz [BDP08]. Hence newly developed MWA devices work at frequencies below 1 GHz and use several applicators at the same time.

### Devices

As mentioned before, MWA devices for patient treatment has only applied in Asia so far. Figure 1.4 (left) shows a japanese MW generator with generating power of 150 W. The chinese device (UMC-I Ultrasound-Guided Microwave Coagulator, Institue 207 Aerospace Industry Company, Beijing, China, and Department of Ultrasound of Chinese PLA General Hospital, Beijing, China) with generating power up to 80 W [dLea01, BDP08]. Both operates at 2.450 MHz emission frequency.

### Electrodes

The japanese system uses electrodes with 1.6 mm in diameter and a 2-cm active tip, the chinese system 1.6 mm with a 2.7-cm tip.

#### 1.2.4 Laser Ablation

Laser-induced Thermotherapy (LITT) is another minimal invasive thermal ablative technique. High energy laser radiation is applied through optical fiber directly into the tumor and energy absorption leads to heating and consequently to tissue destruction. Since laser light is used instead of RF, MR imaging is compatible with LITT devices. This circumstance assures real-time monitoring of the status of the intervention, due to the good soft-tissue contrast and high spatial resolution of MR imaging. Another advantage is the preservation of a well-defined area of necrosis around the fiber tip and thus minimal damage is done to the surrounding tissue [MV08].



Figure 1.4: Microtaze (Heiwa, Osaka, Japan) and needle electrodes. Taken from [ea00]

Although LITT is a suitable technique for local tumor destruction within solid organs, it is mostly used for the destruction of primary and secondary liver tumors.

### Technique of Laser Ablation

Laser light with a wavelength between 1060 and 1200nm is transmitted through a MR-compatible probe to the tissue which leads to coagulation necrosis [ea05b]. Photons of this wavelength have a deep penetration depth. The penetration depth of photons is not only dependent on the wavelength, but also dependent on the tissue. The interaction between biological tissue and laser light is controlled by many physical phenomena, but at these small amounts of energy, that is used in LITT, only scattering and absorption have effective influence on the process. Thanks to the effect of thermal conduction, the temperature extends into the tissue. The laser light itself is transmitted via optical fiber. The applicator holds magnetite markers to allow easier visualization and positioning during the intervention [MV08].

### Devices

Most LITT devices use a neodymium: yttrium-aluminum-garnet (Nd:YAG) laser source. Devices differ in design, types and size of optic fibers, probe tip design and the number of applicators. The MediLas 5100 (Dornier MedTech)



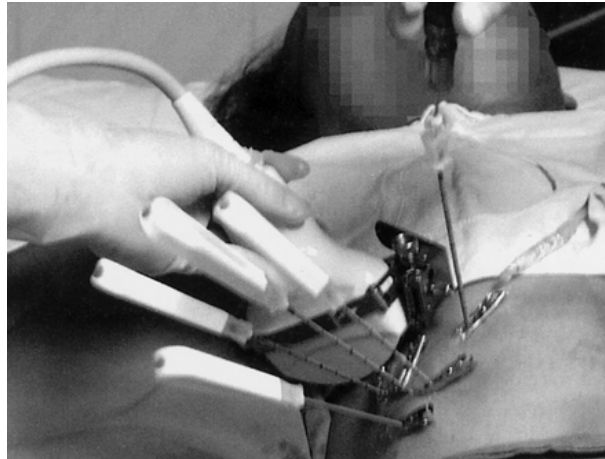


Figure 1.5: "Multiple electrode insertion technique. Five guiding needles are inserted, then microwave energy is applied with one needle at a time." Taken from [dLea01]

uses Nd:YAG lasers with a wavelength of 1064nm. The laser is delivered through a specially developed flexible diffusing applicator.



Figure 1.6: Dornier MediLas 5100 laser system. Picture taken from [imga]

### 1.2.5 High-intensity Focused Ultrasound

High-intensity focused ultrasound (HIFU) is currently studied as a potential method for noninvasive destruction of localized tumors. The main advantage of using HIFU is the noninvasiveness of this treatment. With a transducer ultrasound creates a focused energy beam from the distance. Ultrasound, as form of vibrational energy propagates through the tissue as a mechanical

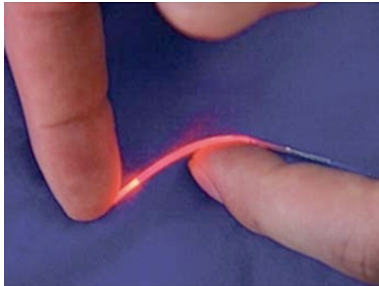


Figure 1.7: The MediLas 5100 flexible applicator. Picture taken from [imgb]

wave. At the targeted point, the beams interfere in a hot spot and result in coagulation necrosis.

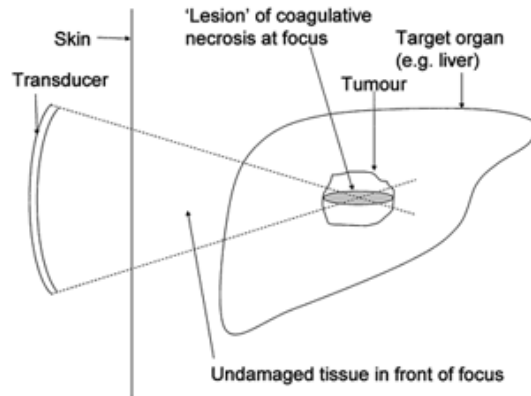


Figure 1.8: Schematic of HIFU treatment. Ultrasound is bundled in a focal point, where it results in heating. Image taken from [JGD03]

### 1.2.6 Shapes of Ablation Zones

Probe	Number of Applicators	Shape	Technique
Cool Tip	single needle <sup>1</sup>	ellipsoid <sup>1</sup>	RFA
Cool Tip Cluster	cluster electrodes <sup>1</sup>	ellipsoid <sup>1</sup>	RFA
LeVeen	multi-tined electrodes <sup>1</sup>	spherical <sup>1</sup>	RFA
Starburst XL	multi-tined electrodes <sup>1</sup>	pear <sup>1</sup>	RFA
Rita	perfused Talon needle <sup>1</sup>	pear <sup>1</sup>	RFA
Celon (Olympus)	single needle <sup>1</sup>	ellipsoid <sup>1</sup>	RFA
Microblate	single electrode	spherical <sup>2</sup>	MWA
Microtaze	single electrode	ellipsoid <sup>3</sup>	MWA
IceSeed	single needles	spherical <sup>4</sup>	CA
IceSphere	single needles	ellipsoid <sup>4</sup>	CA
IceRod	single needles	ellipsoid <sup>4</sup>	CA
IceBulb	single needles	bulb <sup>4</sup>	CA

### 1.2.7 Requirement for a Planning Platform for Thermal Ablation

Thermal Ablation Techniques are gaining popularity as a complementary choice of therapy for different tumors. Although it is commonly considered a safe and low-risk technique, it still suffers from a noticeable rate of complications. A review showed that complication rate of RFA for liver tumors are higher than previously assumed [Mea02]. RFA treatments still has higher tumor recurrence rate than surgical resection. The procedure is more complex as it appear at first. It is not simply inserting a needle and "cook" the tumor [ea04]. The treatment outcome of an intervention is highly influenced by different factors:

- The placement of the applicator(s) is by far the most time-consuming part of the process. Tumors larger in size or multiple small tumors require repeated applicator placement and ablation. However the accurate placement is essential for the efficient treatment.
- The imaging modalities for the guidance of the applicator placement and monitoring the developing ablation zone. Ultrasound is the most frequently used modality, but it is inadequate for imaging the ablation zone accurately [Sch10]
- Larger tumors require lager ablation zones, but this is accompanied by loss of control with an increased rate of damage to healthy tissue.

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<sup>1</sup> [Hel08]

<sup>2</sup> [JON12]

<sup>3</sup> [mic]

<sup>4</sup> [cry]

- Tumors adjacent to large vessels are more difficult to ablate completely since the blood flow acts like a heat sink (see heat sink effect).
- Since thermal ablation techniques are technology-based treatments, the outcome is highly dependent on the wide variation of probe devices, imaging modalities and experience of the operator with these technologies.

The accurate estimation of the ablation zone and treatment result is essential for the success of the intervention. Due to the fact that the above mentioned factors has great influence on the outcome of a thermal ablation intervention, it can be assumed that using a Planning Platform for Thermal Ablation Techniques will positively affect the outcome. This system estimates the ablation zone based on the patient-specific anatomy using 3D visualization and virtually place applicators.

### 1.2.8 Conclusion

Thermal ablation techniques have been developed within the last years as technological advances were made. They are used in clinical practice for the treatment of different localized tumors. Shorter hospital stay, lesser complication during the procedure compared to surgical resection are some of the advantages of these techniques.

Radiofrequency Ablation is the most commonly used technique, followed by Cryoablation and Microwave Ablation. Each technique has advantages and disadvantages. However there are still very little textbook knowledge for education and practice available [Sch10]. In addition the theoretical work of the simulation of the ablation zone is advanced (e.g. see FEA), but they use generic models instead of taking the patient's anatomic structure into account [Sch10]. Due to these circumstances and the strong interconnection between medical practice and technology is most likely that benefits from treatment simulation can be derived.

## Chapter 2

# Requirement Analysis

### 2.1 Introduction

A platform that is targeted to plan the thermal ablation procedure needs to fulfill a minimum set of features. The finished application should help the operator to plan the intervention. But besides the basic functional requirements there is also the non-functional features. As in all software projects, these are as important as functional features. Especially when it is used in clinical practice, it has to meet usability and formal requirements. All organizational and formal requirements would go beyond the scope of this thesis and therefore will not be examined in detail.

Dr. Wolfgang Schramm has reviewed the requirements on such a system in his PhD thesis and therefore the planning software is mostly based on the requirement analysis did by him. He discussed in his PhD thesis the problem between accurate forecast of the treatment outcome and usability. He describes the use of FEA (Finite Element Analysis), that simulates the treatment outcome of thermal ablation, but the additional medical benefit is still not studied [Sch10]. Furthermore the detailed simulation requires high computing power, which leads to a very time-consuming process. That makes distinct forecast not feasible to perform during or immediately before the intervention [Sch10].

### 2.2 Functional Requirements

#### 2.2.1 Image Analysis, Image Processing and Visualization

Thermal ablation is a image-guided therapy and therefore imaging plays a main role in the application. Given that the simulation is based on the patient specific data, the application has to load the data in order to simulate the intervention adequately. Since DICOM (Digital Imaging and Communication in Medicine) is an open standard, that is implemented by nearly all

manufacturer of medical imaging devices, the application must load at least DICOM volumes. For further using, the DICOM volume has most likely to be post-processed. The physician needs to perform simple image processing algorithms to image registration and segmentation for high quality treatment planning [Sch10].

The visualization of the structures is essential to view and interpret the outcome of the treatment. Due to this fact, visualization makes a major part of the functionality of the application. Not only the segmented structures, but also the 3D model of the applicator and the virtual resulting ablation zone has to be visualized.

### 2.2.2 Treatment Simulation

The main function of the tool is to make an adequate forecast of the treatment outcome. Since the resulting ablation zone is highly depend on the used devices, it is necessary to use 3D models of the real devices for the simulation. Thus one of the main requirements is to make sure that the operator can use the 3D model devices with the same properties as the real ones.

The actual ablation outcome is very hard to forecast due to the perfusion mediated temperature change during the ablation [Sch10]. As mentioned in the introduction of this chapter, FEA can be used to simulate the outcome accurately, however this time-consuming technique is not feasible for clinical practice. Instead, the application must be able to visualize the ablation zone based on the estimated values for the coagulation zone dimensions from the respective vendor or from literature [Sch10]. Depending on the ablation technique the shape of the ablation zone must also considered for more accurate estimation. Using this approach regarding the estimation of the resulting ablation zone might not be as accurate as the FEA approach, but this is considered accurate enough to provide valuable information in the planning phase [Sch10].

Ablation techniques like CA uses multiple applicators which results in overlapping ablation zones. This must also be considered during the planning phase. The application must be able to place multiple probes and ablation zones. Afterwards, the visibility of the single ablation zones must be controllable for the operator. Additionally the operator must be able to select the exact entry points on the skin and the targeted points within the tumor.

After placing the probes and drawing the ablation zones, the operator must be provided with visual feedback. Because of preceding segmentation he now can see e.g. if a bone structure lies within the trajectory path or if large vessels lie within the ablation zone.

## 2.3 Non-functional Requirements

The planning platform could either be used in clinical or research environment. In both scopes it must fulfill some formal requirements. By Austrian law, software is declared as medical product and therefore it must fulfill all regulations and can only be used in a clinical environment when they are CE (Conformité Européenne) certified. These certification processes are associated with additional quality assurance requirements and development costs. Since this application is a prototype, the application will disregard these requirements and the non-functional requirements limit to usability.

## 2.4 Conclusion

For creating a planning platform, that considers the patient specific anatomy, it has to take the requirements described in this chapter into account. Considering these requirements the platform has to support several technologies. Instead to develop a standalone application, the software framework Slicer 3D was chosen as the basic application. Using Slicer avoids many unnecessary work, since it already implemented the basic requirements and further it allows to integrate own functionality.

Those requirements that has to implemented as a module for Slicer are specified as user stories (see figure 2.1).

**#1** As an IR, I want to add an insertion radius around the tumor into the scene so that I can choose an adequate entry site for the probe.

**#2** As an IR, I want the insertion radius to be visualized as a transparent sphere so that the region of interest around the tumor is defined.

**#3** As an IR, I want to choose entry points that lie within the sphere, but outside the patient's body so that the virtual probes can be inserted there.

**#4** As an IR, I want to select the same device for the simulation as during the actual intervention so that I can better foresee the results of the procedure.

**#5** As an IR, I want to place multiple virtual applicators into the scene so that I can simulate the real conditions.

**#6** As an IR, I want to see the simulated resulting ablation zone based on the data of the respective device manufacturer so that I can see whether the tumor is fully covered or any other anatomical structures were affected.

**#7** As a developer, I want to easily add new / change devices through an xml document so that I don't have to change the source code of the module.

IR = interventional radiologist

Figure 2.1: Requirements on the platform specified as user stories.

## Chapter 3

# Planning Software Prototype for Supporting Thermal Ablation Interventions

### 3.1 Introduction

The software platform has to be implemented by extending Slicer's functionality. As discussed before, Slicer already implemented the basic functionality and has a wide range of additional functions. One does not simply develop a module for Slicer. The first and most important point was to make sure, that it is possible to implement the requirements as a module for Slicer. By using the research done by Dr. Schramm, the choice for Slicer was from the start clear. Before starting the implementation the developer must engage with Slicer's architecture. Therefore the first part of this chapter describes the technologies used in Slicer, that is relevant for the development of the module. The second part describes the resulting tool.

### 3.2 Slicer

#### 3.2.1 Introduction

Slicer is a free and open source software platform for medical imaging and visualization distributed under a BSD License. Slicer started as a master thesis in 1998 and since then it was mainly developed by the Surgical Planning Laboratory (SPL), which is part of Harvard Medical School. The current Version is Slicer 4.1 released in April of 2012 and it is cross-platform (Windows 7, Mac OS X, Linux).

The code base of Slicer consists over a million lines of (mostly C++ and Python) code [sli11]. It has many funders (National Institute of Health, National Alliance for Medical Image Computing, Biomedical Informatics



Research Network etc.) and partners (Isomics Inc., Kitware Inc. etc.) who enables the ongoing development of Slicer [sli11].

### 3.2.2 Slicer 4 Architecture

Slicer uses the Model-view-controller (MVC) paradigm for its architectural design.

- Model: MRML (Medical Reality Markup Language)
  - the XML-based data model of Slicer
  - MRML-nodes describe the scene and application state
- Controller: Logic
  - creates and manages MRML-nodes
  - Slicer internals, VTK, ITK etc.
- View: GUI
  - User Interface (Qt)
  - Renderers

One of Slicer’s main functionality is its expandability. It is highly flexible and modular, therefore easy to extend its functionality. A large number of toolkits are integrated into the architecture, e.g. the Insight Segmentation and Registration Toolkit (ITK) for image processing, the Visualization Toolkit (VTK) for visualization, Qt for the user interface etc.

### Python

Python is the language for scripting in Slicer. Slicer’s APIs (MRML, Qt, VTK, ITK) are all wrapped. Python has become a very popular scripting language in the past years. But it is more than just a scripting language:

- object-oriented and automatic memory management
- many useful modules included
- widely accepted by the scientific community
- dynamically typed

## Qt

Qt (Trolltech, Oslo, Norway) is a C++ library for cross-platform programming of graphical user interfaces (GUI). In Slicer 3, the GUI was KWidget-based, but it has been ported to Qt since Slicer 4 with the following benefits [sli12]:

- bigger support community since there is a larger number of users and developers
- more training materials available
- design tools (e.g., Qt Designer)
- advanced programming constructs (e.g., signals and slots)
- advanced capabilities (e.g., charting, widgets, SQL interfaces, etc.)
- increased modularity in Slicer

The provided widgets are all automatically wrapped and can be directly used from Python.

## VTK and ITK

The Visualization Toolkit (VTK) can be regarded as the de facto standard for 3D-based visualization in the medical field. It is a freely available C++ library from Kitware, Inc. [vtk12]. It supports a vast number of visualization algorithms and advanced modeling techniques. The module developed in this thesis heavily relies on VTK. For image processing Slicer relies on the Insight Toolkit (ITK) [itk12]. Both Toolkits are widely used by a great number of researchers and developers worldwide.

### 3.2.3 Developing a Module in Slicer

Slicer offers programmers the possibility to extend its functionality by developing modules. The extended functionality will be loaded into Slicer, but will not change Slicer's source base.

There are 3 types of modules supported by Slicer 4.

- Command Line Interface (CLI)  
The simplest way to extend Slicer's functionality is by using the command line paradigm. CLIs are typically used to implement algorithms using ITK.
- Loadable Modules  
Loadable Modules are written in C++ and they are compiled outside of the Slicer build tree. They have full access to the GUI and Slicer internals and are typically used for computationally intensive tasks.

- Scripted Modules

Scripted Modules have full access to the Slicer API via Python, since the libraries (Qt, VTK, ITK, MRML etc.) are fully wrapped. Loadable and Scripted Modules has the same functionality. It is recommended to use Python for rapid prototyping and therefore the Thermal Ablation Module is programmed as a Scripted Module.

### 3.3 Implementation

The challenging part during the implementation was to develop the Module while Slicer 4 was still in development itself (beta phase). Few documentation was available for module developers at this phase, but the mailing list was always very helpful and the subscribers replied very quickly to questions. Like the most open source projects, a mailing list is used for the centralized communication.

The Slicer mailing list is the place where developers and users seek support and discuss other issues. E-Mails sent to the mailing list are automatically distributed to everyone on the mailing list. It is the core team, that provides the major part of support, since they have the best understanding of the software.

#### 3.3.1 Graphical User Interface

Given that the targeted user group are physicians and radiologists, a graphical user interface (GUI) was developed that is both capable to cover all the necessary steps to plan a procedure and user-friendly.

Figure 3.1 shows the GUI of the module. Within section "0: Load Devices XML", the user can load multiple devices into the Slicer. An XML-file is parsed into the Module, but the XML-structure must be both wellformed and valid. To add new devices, the user must edit/write the XML-file manually. The file can be validated against the defined schema (devices.xsd) to check, if the Module can load the file. After successfully loading the XML-file, the GUI will be updated with the new devices. In section "1: Device Selection" the user selects the ablation device he wants to use to plan the procedure. The device with the respective properties such as probe length, probe diameter, size and shape of the ablation zone, is defined in the loaded XML-file. "2: Placement of Insertion Radius" the user can place a sphere around the targeted tumor to visualize the insertion radius. In order to target, the user must place a Fiducial within the tumor. Adding Fiducials to the scene automatically updates the GUI. When the entry point is chosen (by placing another Fiducial), the sphere can be deactivated.

There are two combo boxes visible in section "3: Probe Placement". The first selects the Fiducial of the entry point, where the probe should be

Figure 3.1: The Thermal Ablation module in Slicer 3D.

inserted through the skin. The second selects the targeted Fiducial. By choosing several different Fiducials the user can place multiple probes.

When the probes are placed, the user draws the resulting ablation zone in the section "4: Draw Ablation Zone". The resulting ablation zones caused by the different virtual probes are listed in the last section "Ablation Zones". The user can toggle the visibility of every ablation zone in this section.

### 3.3.2 Structure

#### **ThermalAblationPlanningModule.py**

Includes the creation of the GUI, the basic setup and a major part of the logic.

#### **VTKSourceDrawer.py**

VTK objects, model nodes for MRML scene are created here.

#### **Device.py**

Defines the Device class.

**devices.xsd**

Defines the schema the XML file, that contains the properties of the devices.

**3.3.3 Conclusion**

A planning platform for thermal ablations, that can be used in clinical environment, has to meet a set of minimum features (see chapter 2). The development of such a platform can be done by two approaches. It could be developed as a standalone application, that uses the available libraries or it is going to be developed as an extension to an existing application. Using the second approach has the advantage that many basic functionality are already implemented and this avoids unnecessary work. On the other hand developing an extension could have restrictions when developing the features.

Slicer and its modularity and open architecture was ideal. It already implemented a big part of the minimum requirement of the planning module and provides the possibility to integrate custom functionality. But in order to develop a module for Slicer, it is essential to understand its architecture. Especially the VTK library and Slicer's data model MRML was crucial to understand during the development.

MRML nodes are used to place 3D objects into the Slicer View. Fiducial Points can be placed in order to place the probe and draw the ablation zone. In order to place and orient the 3D geometric objects between the Fiducials, geometric calculations were used. Different devices can be specified through an XML file. Using the VTK library two shapes of ablation zones are currently implemented. It is easy to extend the functionality by adding new ablation zone shapes. A new python class can be added in to the designated module, referred as VTKSourceDrawer.py.

All in all, different techniques and technologies came to use during the development. The completed tool is open source and accessible to Slicer developers. End users can install the module by following the steps described in Appendix A.

**3.4 Using The Module to Plan a Thermal Ablation Procedure****3.4.1 Work Flow**

Figure 3.2 shows the workflow description of a standard planning procedure. The first step is to load the image data into Slicer. The image data has to be prepared for the planning simulation. Tasks like segmentation, registration etc. have to be performed in this step. Since the planning depends on the devices that are going to be applied, these must be loaded into Slicer at the

next step. After selecting the right device, the insertion sphere has to be placed to see evaluate the possible entry points. This follows the selection of the target point. After the drawing of the ablation zone the operator can see whether the tumor is covered by the ablation zone or not. If the tumor is not covered, new target points can be placed and these steps has to be repeated.

### 3.4.2 An Example

See Figure 3.3 for a example of the functionality of the module.

## 3.5 Discussion and Outlook

The planning-software was developed mainly on basis of the requirement analysis depicted in the PhD thesis of Dr. Wolfgang Schramm. Since there was no direct interaction with the medical experts, literature about the process of thermal ablation procedure had to be studied. Another way to get to know the procedure was watching the recordings, that were done by different hospitals in the U.S., e.g. the Wake Forest Baptist Health. These recordings were very insightful, since they showed the entire procedure and allowed others to partake, by asking questions. Nonetheless, the software is limited on the basic functionality to cover the essential steps of the planning phase. If the software is aimed to be used solely in medical environment, it must not only be extended by a large set of additional functionality, but also undergo a strict and costly certification procedure. As mentioned before, this clearly is out of scope of this thesis.

The development of the scripted module for Slicer 4 was not quite as smoothly, as hoped. Particularly the lack of documentation during the beta phase was delaying the development. In addition the development required to deal with various software technologies, such as visualization using VTK, GUI design using Qt, MRML as scene description, Python as scripting language and so forth. These libraries and frameworks are mostly well documented but it took some time to figure out, how to use them in Slicer environment. Due to these circumstances, the development of the module took more time that it would have taken, when it were developed at a later phase of Slicer's development.

As shown in chapter 1, the probes of the respective manufacturer create different shapes of ablation zones. The shapes are usually ellipsoidal or spherical, but also pear shaped zones appears. Given that the real ablation zone depends on many factors (tissue properties, size of tumor, heat sink phenomena, time of temperature exposure, the operators experience etc.) the visualization of the adequate shapes would not only create disproportional large development expenses, but also imply accuracy that the platform can

not guarantee. These shapes are going to be modeled as spheres and cylinders, since they are sufficient approximations of the actual ablation zone shapes.

All in all, the modularity of Slicer’s architecture allowed the integration of custom functionality, therefore unnecessary work was avoided. The resulting application implements the in chapter 2 mentioned requirements and allow to place applicators and show the treatment outcome by simulating the ablation zone on basis of the respective device manufacturer and the patient specific anatomy. This suggest that this tool can not only applied in medical practice but also used for education and practice. Considering the tool, it suggest that especially for educational purposes, the use of a haptic device would make the interaction during the probe placement very realistic. The device would interact with the virtual anatomy of the patient by controlling the probe. The user is able to ”feel” the tissue structure over the device and thereby learn to place an probe in virtual environment.

The functionality can always be extended by interested Slicer developers. Since the development started as an open source project, the source code can be found at <https://github.com/HaichaoMiao/Slicer4-Module>. Github allows an rapid way to fork a project, to work on an own branch of the software.

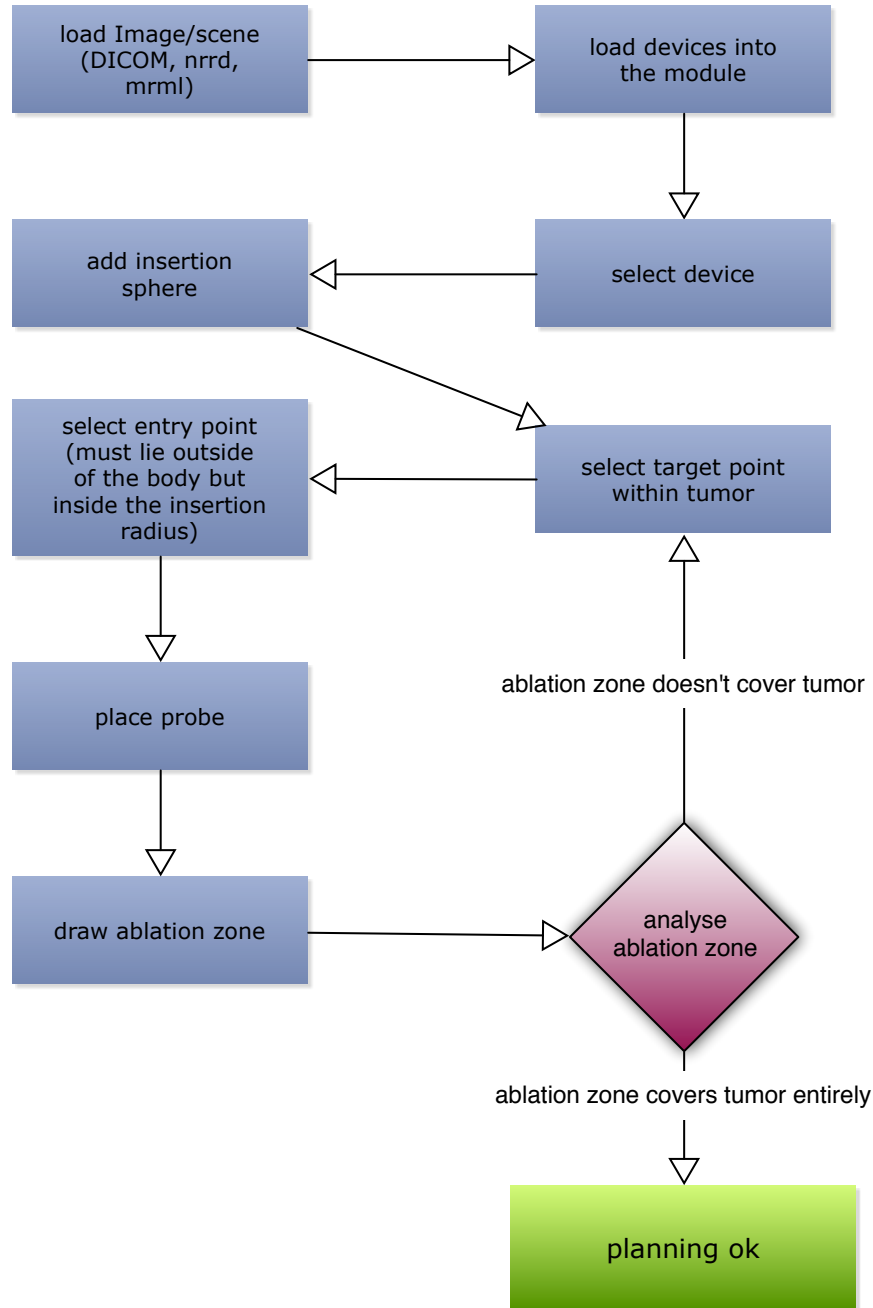


Figure 3.2: Workflow description of the steps that needs to be carried out to plan the intervention.



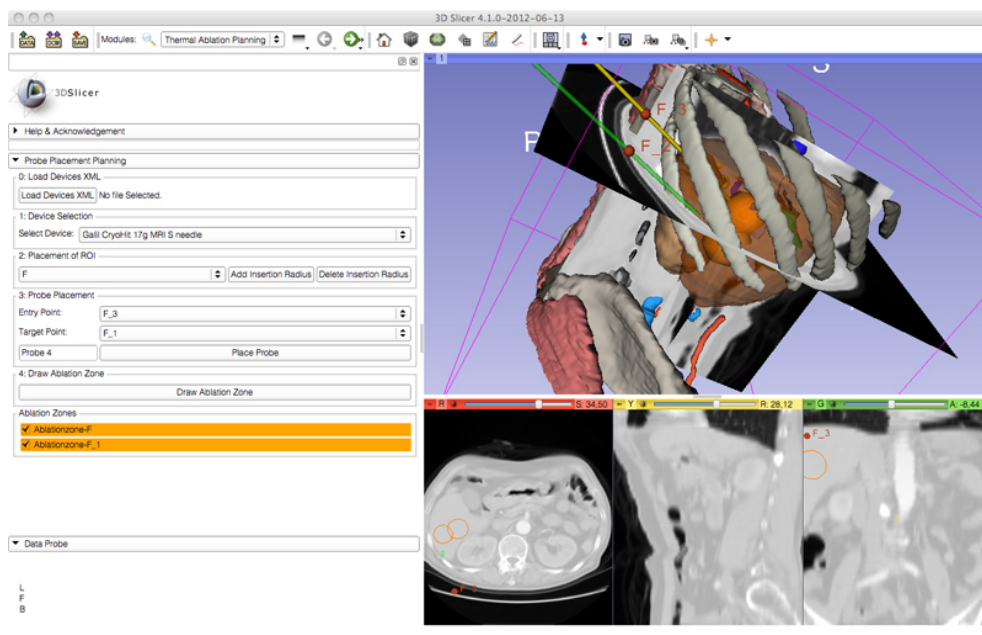


Figure 3.3: 3D Visualization of the abdominal structure. The Simulation of the insertion of Galil CryoHit 17g MRI S needles and two spherical ablation zones.

## Chapter 4

# Conclusio

Over the past years, different thermal ablation techniques have been applied successfully to treat tumors. The treatment of malignant liver tumor, kidney tumor and many other localized tumor forms by using thermal energy sources has gained clinical acceptance. Although tumor patients benefit from the thermal ablation interventions, the treatment itself is still limited by the maximum size of ablation zone, that can be achieved. Thermal ablation is not an alternative to surgical resection but a complementary treatment form.

Before the intervention starts, many decisions have to be made, which have great impact on the treatment outcome. Because of the multidiscipline nature of the treatment form, a planning phase may have major influence on the treatment. Many errors during the intervention, such as wrong applicator placement could do irreversible damage to the patient. The software supports the operators during the planning phase by visualizing the procedure and making an adequate forecast of the treatment outcome. This helps the collaborators to picture and understand the intervention as a whole and thus the prototype helps avoiding errors.

The prototype gives feedback whether the trajectories of the placed probes are applicable or not. Additionally the prototype gives feedback of the coverage of tumor by the ablation zone on basis of the respective vendor or literature. However the developed prototype is far from the actual application in the clinical practice as discussed before, but it makes another step towards the goal of supporting the thermal ablation intervention by software.

## Chapter 5

# Terms and abbreviations

### Acronyms

CA	Cryoablation.
CT	Computed Tomography.
DICOM	Digital Imaging and Communication in Medicine.
FEA	Finite Element Analysis.
HCC	Hepatocellular Carcinoma.
HIFU	High-intensity focused ultrasound.
ITK	The Insight Segmentation and Registration Toolkit.
LITT	Laser-induced Thermotherapy.
MRI	Magnetic Resonance Imaging.
MRML	Medical Reality Markup Language.
MW	Microwave.
MWA	Microwave Ablation.
RF	Radiofrequency.
RFA	Radiofrequency Ablation.
US	Ultrasound.
VTK	The Visualization Toolkit.

## Appendix A

# Download and Install the Toolkit

To use the Thermal Ablation Planning Module, the user must first install the module. The source code can be found at <https://github.com/HaichaoMiao/Slicer4-Module>. The README file contains all the instructions:

Name: Thermal Ablation Planning Module for Slicer 4  
Creator: Haichao Miao  
Date: 20.06.2012  
Version: b1.0  
Language: Python  
Platforms: Slicer 4 (Windows, Mac OS X, Linux)  
=====

This Module provides different tools for the planning phase of a tumor ablation intervention.

I) Getting Started:

Download Slicer <http://download.slicer.org/>

II) Load the "Thermal Ablation Module" into Slicer

Slicer -> Edit -> Application Settings -> Modules ->  
Additional module paths ->  
Add directory path of the file ThermalAblationPlanningModule.py

Restart after adding the path

-----

The main functionalities of this module are as follows:

- 1) add/delete an insertion radius around the tumor
- 2) select target and entry points
- 3) place and orient multiple probes
- 4) visualize the resulting ablation zones
- 5) different ablation zone shapes (currently sphere and cylinder)
- 6) list ablation zones
- 7) toggle visibility of ablation zones
- 8) select devices of different manufacturers with the respective specifications
- 9) define new devices and loading them into slicer

-----

## Appendix B

# Developing a Python Scripted Module

### B.1 The Python Console

To use the Python console within Slicer 4 is a good way to get started with developing a scripted module. The console gives access to Slicer's scene objects, the processing libraries (VTK, ITK, CTK and numpy), PythonQt and most of the standard Python library. Of course to have access, libraries have to wrapped APIs.

Use View - Python Interactor to bring up the console. Python code will be executed here. By pressing the Tab Key the console makes suggestions for command completion, which proved to be very useful.

### B.2 Create an Module Skeleton

A module needs to have a basic structure and description to be executable for the Slicer framework. Instead of writing the module from scratch, which could be confusing at the beginning, the developer can get started by creating a module skeleton, that is already executable and contains the basic description.

To create a Scripted Loadable Module, execute the following code from the Slicer source directory.

```
./Utilities/Scripts/ModuleWizard.py --template  
./Extensions/Testing/ScriptedLoadableExtensionTemplate  
--target ../MyExtension MyExtension
```

- The template option specifies the directory containing a Slicer module.
- The target option defines the directory and the name of the module

The created skeleton already contains the module description and GUI. For setting up Slicer to load the module, please see Appendix A.

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