We are IntechOpen,
the world's leading publisher of
Open Access books
Built by scientists, for scientists

6,900
Open access books available

186,000
International authors and editors

200M
Downloads

154
Countries delivered to

Our authors are among the
TOP 1%
most cited scientists

12.2%
Contributors from top 500 universities

WEB OF SCIENCE™
Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com

Chapter

Stereotactic Image-Guidance for Ablation of Malignant Liver Tumors

Iwan Paolucci, Raluca-Maria Sandu, Pascale Tinguely, Corina Kim-Fuchs, Martin Maurer, Daniel Candinas, Stefan Weber and Anja Lachenmayer

Abstract

Stereotactic percutaneous ablation is a rapidly advancing modality for treatment of tumors in soft solid organs such as the liver. Each year, there are about 850,000 cases of primary liver cancer worldwide. Although surgical resection still is the gold standard for most cases, only 20–30% of patients are candidates for it, due to the advanced stage of the disease. Surgery can also be a huge burden to the patient and his/her quality of life might be temporarily severely reduced due to long hospital stays, complications, and slow recovery. To overcome these disadvantages, thermo-ablation of tumors of up to 3 cm has become a more viable alternative especially in the last decade, offering a potentially equally effective but minimally invasive and tissue sparing treatment alternative. In conjunction with improved CT imaging, stereotactic image-guidance techniques and image fusion technology were introduced to increase safety, efficacy, and accuracy of this treatment. Stereotactic image-guidance leads to a simple, fast, and accurate placement of the ablation probe into the liver tumor, which is a prerequisite for a complete destruction of the tumor by ablation. More and more physicians, including surgeons, consider ablation a viable alternative to resection whenever feasible. Patients undergoing such a minimally invasive treatment benefit from a shorter hospital stays, reduced complication rates, and faster recovery.

Keywords: image-guidance, ablation, microwave/radiofrequency ablation, irreversible electroporation, liver tumors

1. Introduction

Thermal ablation of liver tumors is a minimally invasive locally destructive treatment alternative to surgical resection, which is the current gold standard for curative care. Not only is ablation considered for patients not amenable for surgical resection (<20%) but also increasingly for resectable tumors even with a curative intent [1–3]. Percutaneous ablation is generally performed under image-guidance based on CT, MRI, or ultrasound. Stereotactic image-guidance leads to a simple, fast, and accurate placement of the ablation needle into the liver tumor. Patients undergoing a percutaneous ablation benefit from an improved quality of life due to the shorter hospital stay compared to patients undergoing surgery [1].

The key challenges in percutaneous ablations are complete coverage of the tumor with ablation necrosis including a 5- to 10-mm margin. Insufficient coverage of the ablation necrosis is related to local tumor progression, which is also associated with poor survival prognosis. While there are many unknown factors influencing the ablation process, one of the prerequisites is the accurate placement of the ablation needle in the tumor to ablate the tumor from the inside out. Stereotactic image-guidance aims to provide technical means to plan and accurately place an ablation needle into the tumor and verify its complete destruction.

1.1 Indications

For primary liver tumors (hepatocellular carcinoma, HCC), ablation is considered in cases of very early to early stage disease (BCLC 0/A) with less than three lesions that are smaller than 3 cm in diameter, according to the Barcelona Clinic Liver Cancer (BCLC) staging system guidelines [4]. For liver metastases from colorectal cancer (CRLM), ablation is still mostly performed for lesions not amenable to resection; however, first comparative studies suggest equal oncological outcomes (local recurrence, survival) after ablation versus resection of potentially resectable lesions [5]. The application as alternative to resection for HCC > 1 cm and CRLM is currently studied in various clinical trials; however, the oncologic non-inferiority of ablation has still to be confirmed in prospective trials. While the guidelines do not specify the access (open surgical vs. laparoscopic vs. percutaneous), it has been shown that the percutaneous access has lower complication rates and hospital stay with similar oncologic outcomes. Therefore, percutaneous ablations are generally preferred over surgical ablations. However, surgical ablations are performed in lesions that are difficult to target percutaneously or when ablation is combined with surgical resection. Stereotactic image-guidance offers a procedure to accurately target a lesion percutaneously, even in very difficult cases, in a predictable time.

In recent years, studies have been conducted to show that stereotactic image-guidance also allows to treat larger lesions by combining multiple ablation zones to fully cover the lesion [6], and also as an option for downstaging or bridging candidates for liver transplantation [7]. Larger lesions can also be treated with transcatheter arterial chemoembolization (TACE), but complete necrosis is barely achieved due to incomplete embolization and tumor angiogenesis. Therefore, approaches have been studied where TACE is combined with thermal ablation for HCCs >3 cm and found a synergetic effect [8]. For this combined treatment approach, an image-guidance approach has also been proposed, and preliminary animal experiments conducted [9].

1.2 Available image-guidance systems

There are currently three stereotactic image-guidance systems available on the market. The CAS-One IR (CAScination AG, Switzerland) and IMACTIS (IMACTIS, France) systems are pure image-guidance systems, whereas the MAXIO (Perfint, India) is a system with an integrated robotic arm for needle alignment. There are also several research devices in use in specialized clinics and it is expected that more devices will be available in the future.

1.3 Ablation modalities

Tumor ablation is defined as the local delivery of thermal, chemical, or electrical energy to a specific tumor in order to achieve its complete destruction. The most commonly used ablation techniques in conjunction with stereotactic image-guidance are thermal, chemical, and electrical ablation, which are described in the following sections.

1.3.1 Thermal ablation

Radiofrequency ablation (RFA) refers to energy sources that generate energy within the RF spectrum between 300 and 500 KHz. The RF electrode destroys all the cells at the target zone by heating up the tissue as a result of a high alternating electrical field that oscillates in the high-frequency range [10]. In Microwave ablations (MWA), a high-frequency electromagnetic field in the range of 900 MHz–2.45 Ghz forces water molecules to continuously realign, which results in high kinetic energy that is converted to heat in the tissue. Both RFA and MWA techniques destroy the tumor cells by coagulation necrosis using heat above 60°C. Compared to RFA, MWA heats the tissue faster due to the different heat distribution and therefore is also less affected by adjacent vessels (heat sink effect) [11, 12].

To date, most evidence supporting local ablation for small HCC lesions is based on works reporting RFA treatment and the comparison of RFA versus surgical resection. However, more recently, the theoretical and clinical advantages of MWA have often been highlighted. These include shorter application times, and the generation of higher temperatures resulting in larger ablation zones. Currently, several works comparing RFA versus MWA have reported partially contradicting results, especially regarding local tumor control after bot treatments [13, 14]. Overall, it can be assumed that no significant difference between RFA and MWA regarding overall and recurrent-free survival in patients with HCC exists [15]. However, there seems to be a tendency toward superiority of MWA regarding local recurrence rates in larger tumors as well as regarding operating times.

Cryoablation destroys tissue with freezing temperatures, alternating freezing and thawing or slight heating. The rapid freezing of tissue disrupts the cellular membranes by direct intracellular ice crystal formation. The most commonly used cooling agents are argon gas or liquid nitrogen [16].

1.3.2 Chemical ablation

Percutaneous ethanol injection (PEI) is the most commonly employed chemical ablation technique, but was demonstrated to have inferior results to thermal ablation [17]. PEI denaturizes the cellular proteins through cytoplasmic dehydration, which eventually also causes local coagulation necrosis. However, when compared to the other techniques, PEI shows significant disadvantages such as high local tumor progression rate, unpredictable ablation volumes, and lower overall survival rates.

1.3.3 Irreversible electroporation

Irreversible electroporation (IRE) is non-thermal ablation technique that delivers short pulses of high-voltage electrical energy directly to a tumor. This technique disrupts the cell membrane irreversibly and induces cell death by apoptosis (also known as natural cell death). The advantage of IRE is that it preserves blood vessels and therefore there is a high incentive to use IRE especially where vital structures and blood vessels can be easily damaged by thermal ablation methods [18]. IRE requires placing multiple needles in parallel and at a specific configuration and distance and therefore stereotactic image-guidance provides a precise placement of the needles. As IRE is a relatively new treatment, there are also less data available about its outcomes.

2. Components of a stereotactic image-guidance system

In this chapter, the general components of stereotactic image-guidance devices are described. In general, such a system consists of (**Figure 1**):

a. a tracking system that measures the position and orientation of the patient and the instruments in 3D space

b. software packages for

- trajectory and ablation planning
- trajectory and ablation validation
- visualization aids for needle placement

c. an alignment device that allows an accurate placement of the ablation needle into the tumor

2.1 Tracking systems

The tracking system measures the position and orientation of the needle guidance device and the patient in space. There are currently two different tracking modalities used for these procedures, namely optical and electromagnetic tracking. Optical tracking systems use a stereo infrared camera and locate retroreflecting spheres mounted on a rigid body— the so-called marker shields. Based on the geometry of these marker shields, the camera is able to identify them (e.g., needle guidance device). The second tracking modality is electromagnetic tracking, which generates an electromagnetic field and measures the current induced into small coils, which are attached to the device [19]. The position and orientation of the instrument are calculated from the current and a chip attached to the sensor provides information for identification.

Figure 1.
Components and setup of a stereotactic image-guidance system.

Optical tracking systems tend to be more accurate but have the problem of a line-of-sight. Therefore, if the line-of-sight is occluded (e.g., by blood, radiologists' hand), the tracking device will lose track of the marker. Electromagnetic tracking relies on a known magnetic field and therefore is heavily affected by ferromagnetic and electrically conducting materials. Therefore, which system to use heavily depends on the target environment where the system will be used.

2.1.1 Patient tracking

A stereotactic image-guidance system needs to know where the patient is located relative to the tracking device in order to calculate the position of the needle guidance device relative to the planned needle trajectory (**Figure 2**). One option is to place retroreflective spheres on the patient that are detectable by the optical tracking system [20]. These spheres are also detectable on the CT scan and can therefore be used to register the CT to the patient [21]. Another approach, typically used with EM-based systems, is to place a position sensor on the patient's abdomen, which can be detected by the EM-tracking system. Both methods allow to track the patient in space. However, organ deformations due to breathing or repositioning of the patient cannot be calculated by these tracking methods. Nevertheless, when using multiple spheres or sensors, large deformations can be recognized, which allows to display a warning to the user.

2.2 Navigation software

The navigation software consists of planning tools, validation tools, and visualization aids for the radiologist to accurately align the needle guide and place the ablation needle.

2.2.1 Trajectory and ablation planning software

With the trajectory planning component, the radiologist plans trajectories to the tumor and also estimates the amount of energy needed to successfully ablate the tumor. In the most basic form, the software allows to plan a single straight-line trajectory to the tumor. In a more advanced setting, the software compensates for the offset between the needle tip and the active zone (which depends on the type of ablation device) and also supports multi-needle ablations with overlapping ablation

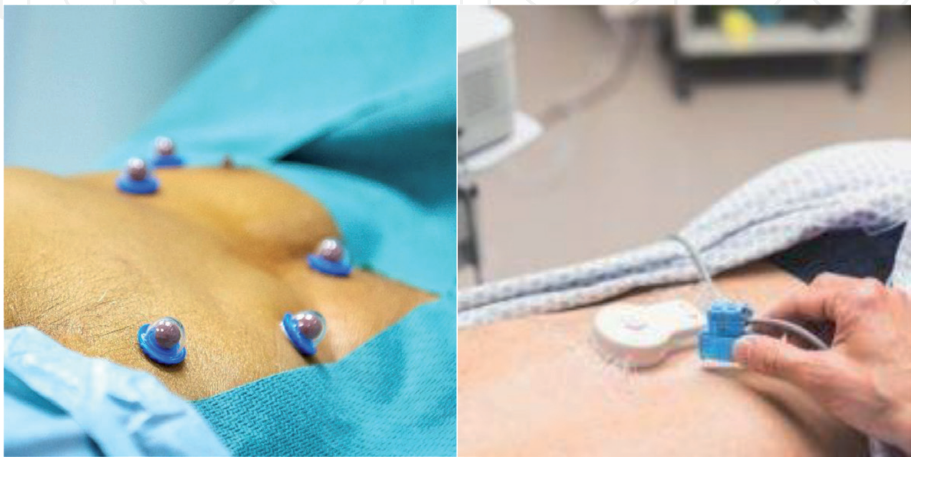

Figure 2.
(left) Patient tracking method using multiple retroreflective spheres (right) or using a single EM position sensor (© IMACTIS).

zones [6]. A trajectory for an ablation consists of a target point (tumor center) and an entry point on the skin. Depending on the location of the tumor, this trajectory passes nearby critical structures (e.g., *major* blood vessels, ribs) where specialized views along the needle trajectory are used to keep sufficient distance from these structures.

In cases where the tumor is not visible on the CT scan or the contrast agent cannot be administered to the patient, a pre-operative MRI scan can be fused with the intra-operative CT. The image-guidance system then allows to plan the trajectory on the MRI scan and then calculates the location on the CT scan.

2.2.2 Navigation visualization

The visualization component for navigation typically consists of a crosshair viewer and/or CT slice with a real-time overlay of the needle trajectory. This allows the radiologist to align the needle guidance device with the planned trajectory and then to place the needle at the correct depth. An indication of the deformation or motion of the patient is also visualized for monitoring and estimation of the accuracy.

2.2.3 Ablation validation

The ablation validation component fuses the pre- and post-ablation CT scans and visualizes them using alpha blending. The radiologist can switch between the pre- and post-ablation scan by choosing the blending level. More advanced systems allow to segment the tumor and the ablation zone and present a coverage.

2.3 Needle guidance devices

2.3.1 Freehand stereotactic navigation

With freehand navigation, a position sensor is attached to the ablation needle and the position and orientation of the needle are measured by the tracking device. The radiologist can freely move the needle and the navigation screen helps to place the needle according to the defined plan.

2.3.2 Stereotactic arms

When using a stereotactic arm (**Figure 3**), the tracking device measures the position and orientation of the needle guide in the stereotactic arm and uses this information to guide the radiologist. Such an arm typically has multiple handles, which allow to adjust and lock each degree of freedom separately. With this, the radiologist first aligns the arm roughly to the entry point on the skin and then pulls the handle to lock the position of the stereotactic arm. The remaining handles can then be used to fine-adjust the orientation to exactly align the device to follow the planned trajectory. Once the trajectory is aligned, the needle can be placed through the needle guide with the depth that is indicated on the navigation screen [22].

Another advantage of the stereotactic arm is that it holds the needle in place during a control CT scan and during the ablation procedure. This prevents movement of the needle, which would result in an uncontrolled ablation and potential tissue damage. Because the stereotactic arm holds the ablation needle during the control CT scan, the radiologist does not need to be in the CT room and thus is also not exposed to radiation [23].

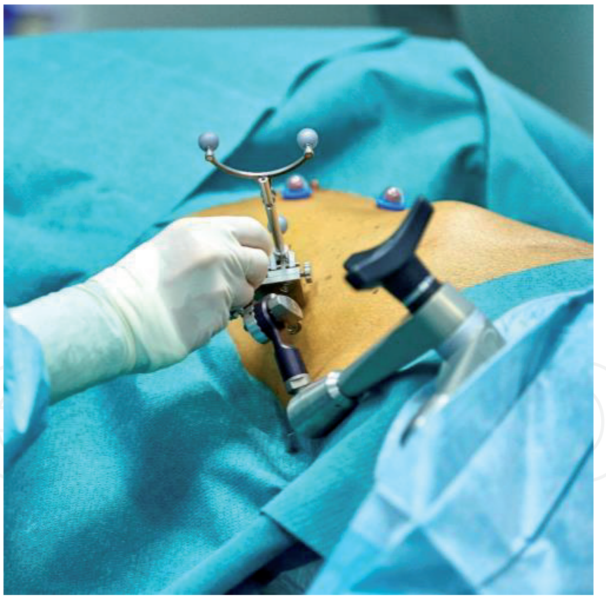

Figure 3.
Stereotactic arm during the adjustment of the needle trajectory.

2.3.3 Robotic devices

These devices are motorized articulated arms for alignment of ablation needles, providing a 6-dimensional alignment of a trajectory with respect to the target. The radiologist delivers the needle by hand and the robots passively guide it. There is a commercial provider, which has shown superior results in terms of accuracy and precision when compared to freehand targeting [24]. The findings from pre-clinical models and also from available clinical data show that passive needle guidance robots do not significantly increase available accuracy compared to stereotactic arms. Therefore, it is rather a matter of choice which kind of system to use.

3. Procedure

In the following chapter, a typical workflow (**Figure 4**) for a stereotactic image-guided percutaneous ablation of a liver tumor is presented.

3.1 Patient preparation

An important part when applying stereotactic guidance is that the organ of interest is properly fixated. In the case of the liver, that not only means to fixate the patient but also reduce the motion of the liver due to breathing. The fixation of the patient is generally done using a vacuum mattress. Once the patient is under

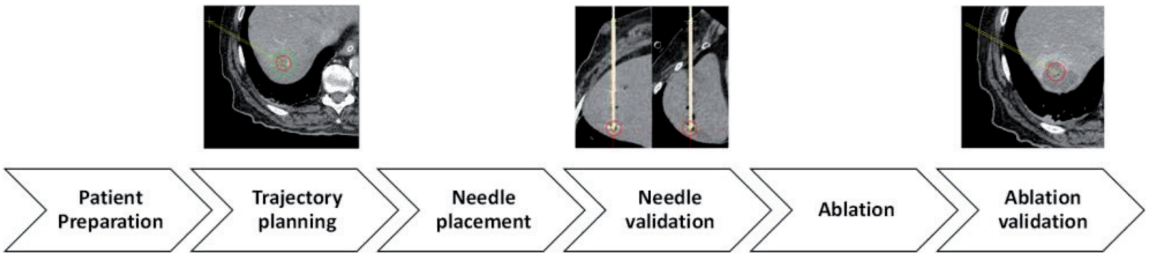

Figure 4.
Workflow of a percutaneous ablation of a liver tumor using stereotactic image-guidance.

anesthesia, the vacuum mattress is pressed toward the patient and the vacuum applied. This will prevent the patient from moving on the CT table.

To minimize the motion of the liver due to breathing, there are a number of alternatives:

- *Apnea*: where the ventilation is stopped on the ventilation device to hold a predefined air pressure inside the lung.
- *Tube disconnection*: where the endotracheal tube is disconnected from the ventilation device and all air is exhaled from the lungs.
- *High-frequency jet ventilation (HFJV)*: where short pulses of small volumes of pressurized air are delivered with high respiratory rates. This technique of mechanical ventilation results in minimal movement of lung and abdominal organs and is feasible for long durations [25].

Apnea and tube disconnection are applied during the CT scans and during the needle placement, while during the rest of the procedure, normal ventilation is applied. Jet ventilation can be applied during the whole procedure or also only during the CT scans and the needle placement.

3.1.1 Marker for patient tracking

Before starting the procedure, the patient tracker has to be placed on the patient's abdomen. Depending on the system, there are also specific requirements on how and where to place these markers for optimal accuracy of the system.

3.2 Trajectory planning

A trajectory for an ablation consists of a target point (the center of the tumor) and an entry point (entry on the skin) (**Figure 5**). Most ablation systems do not have their active center (the center of the ablation) at the tip. Therefore, the ablation system and the needle type can be selected, and the navigation system then computes a modified trajectory, such that the center of the ablation is in the center of the tumor. Additional to the trajectory, software guidance can also support the decision of the time and energy level to apply during the ablation. To avoid the puncture of

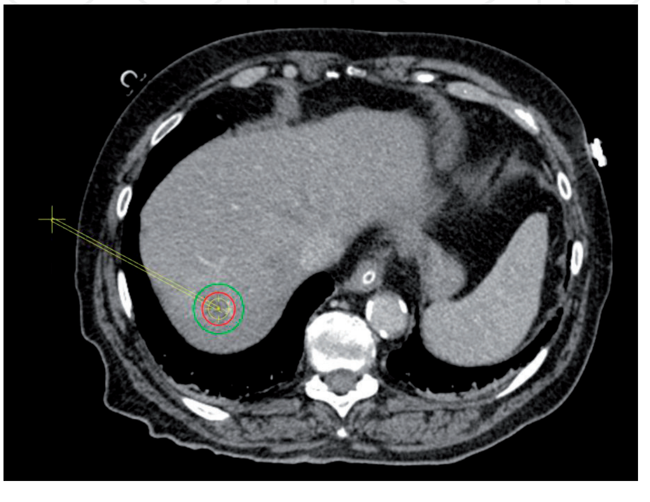

Figure 5.
Planning of a trajectory and the optimal ablation energy through an inter-costal trajectory.

blood vessels or other organs at risk, the navigation system presents a slice of the CT scan along the planned trajectory. This is especially useful in ablations in the superior segments where usually a sub- or inter-costal trajectory is required.

In case the tumor is not visible on the CECT scan, a pre-operative MRI scan can be fused with the intra-operative CT scan. The trajectory can then be planned on the MRI scan and the navigation system calculates the position of the trajectory on the intra-operative CT scan. One thing to consider is that the liver might have deformed with respect to the MRI scan depending on the positioning of the patient. Therefore, it is crucial to visually assess the accuracy of the fusion before planning a trajectory.

3.3 Navigated needle placement

During the navigated needle placement, the radiologist aligns the stereotactic arm with the planned trajectory according to the crosshair viewer. Additionally, the system presents a real-time overlay of the needle trajectory on the CT scan (**Figure 6**). Once the stereotactic arm is aligned, the needle can be placed into the tumor according to the depth information on the display.

Depending on the patient tracking method, the system presents a real-time estimation of the deformation of the organ and stops the navigation display if the estimated deformation is too large.

3.4 Needle validation

To ensure correct needle position before applying the energy of the ablation needle, a non-enhanced CT scan is acquired and fused with the planning scan by the navigation system. The image-guidance system then either detects the needle automatically or the radiologist selects it manually. Based on this selection and the planned trajectory, the needle placement accuracy is measured and displayed on the screen (**Figure 7**). If the placement accuracy is insufficient (>3 mm), the radiologist would repeat the needle placement step.

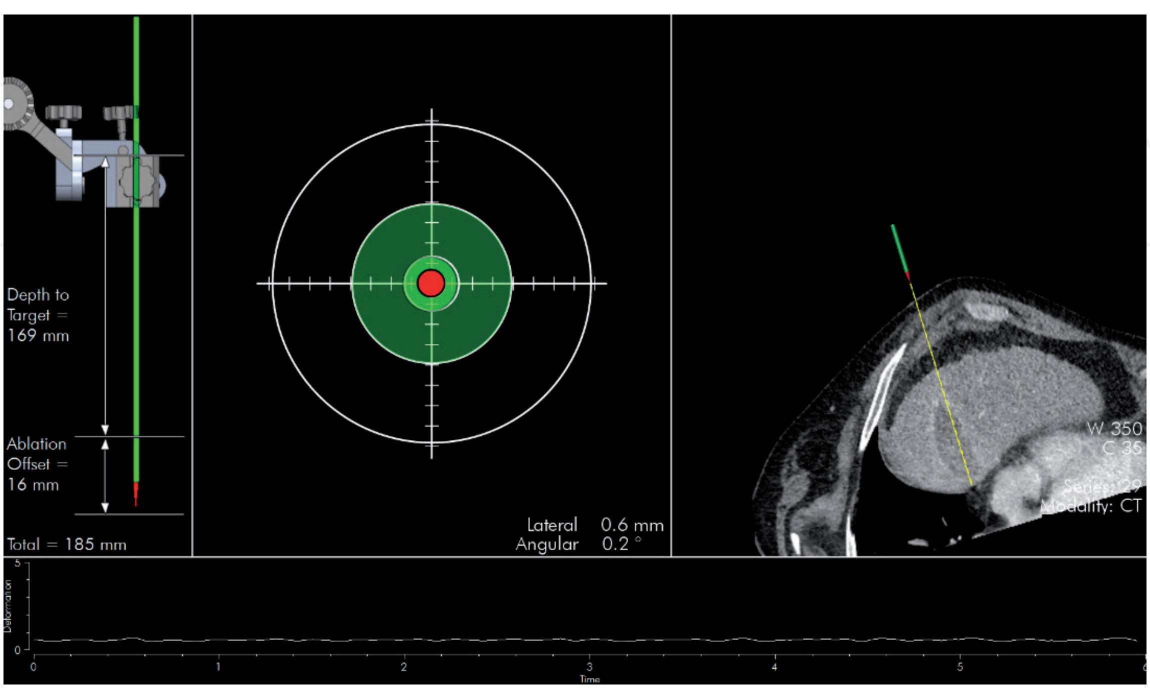

Figure 6.
Crosshair viewer with the orientation and depth aid for accurate placement and a real-time CT slice along the current trajectory.

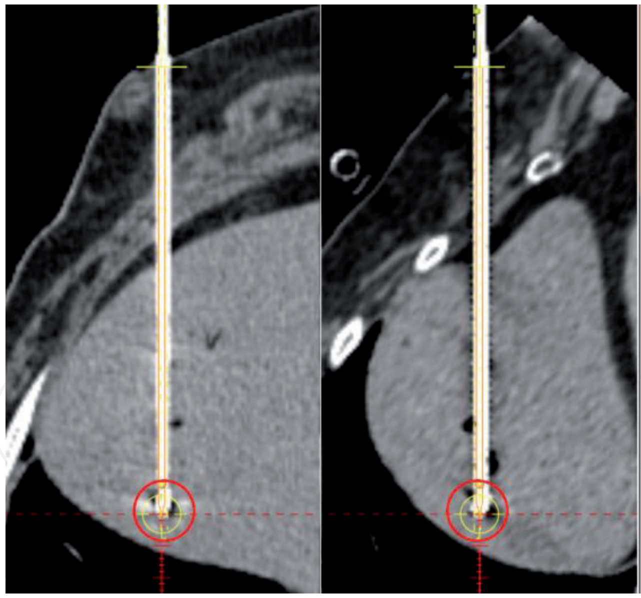

Figure 7.
Needle validation on a CT slice along the actual needle trajectory.

In lesions that are close to critical structures (vena cava, heart, etc.), the needle can be placed at three-fourths of the final depth and correct orientation can be measured on the needle validation scan before the needle is inserted into the final target.

3.5 Ablation

Once correct needle placement is confirmed, the energy is applied by the ablation device. The amount of energy needed can also be planned with the planning software. However, recent studies have shown that the resulting ablation zones differ from the prediction based on the ex-vivo results that are provided by the ablation device manufacturers [26] and also depend on the tumor type [27].

3.6 Ablation validation

In this step, the radiologist evaluates the coverage of the tumor by the ablation necrosis, which has been shown to be an independent predictor in determining local

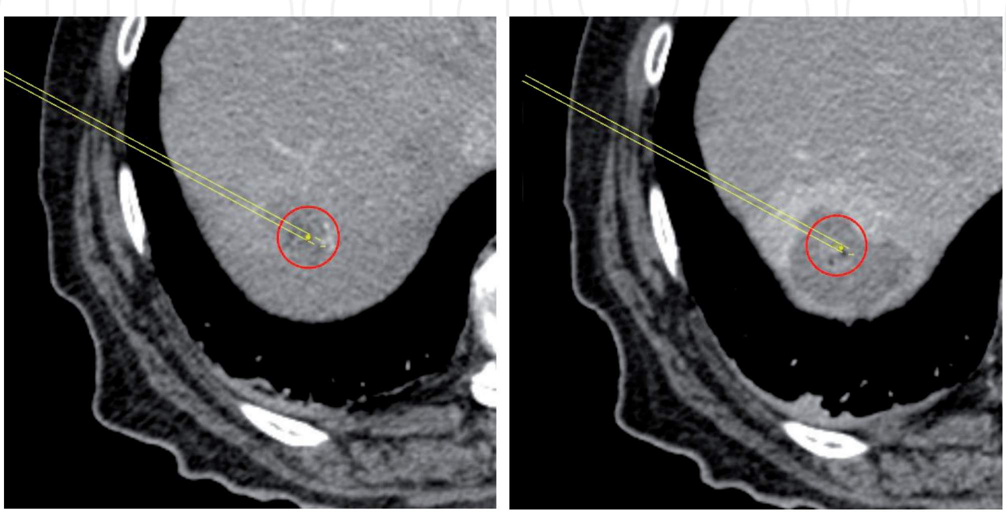

Figure 8.
Ablation zone validation with the tumor on the pre-ablation scan (left) and the ablation necrosis on the post-ablation scan (right).

tumor recurrence with a larger ablation margin resulting in a lower risk of local tumor recurrence [28]. The ablation coverage and margin are evaluated by visual assessment where the radiologist compares the pre- and post-ablation scans, which can be displayed side-by-side on a radiological screen or overlaid with transparency (**Figure 8**). An image-guidance system or external software can display the segmented tumor and the planned ablation margin, which makes the visual ablation validation more accurate, reproducible, and less subjective by providing visual markers and boundaries. If the radiologist identifies residual tumor or insufficient margin on the fused pre- and post-ablation scan, then another ablation is performed in the same procedure. Therefore, a new trajectory is planned based on the post-ablation scan to also cover the remaining tumor.

4. Current evidence and future perspectives

Using stereotactic ablation reduces the exposure to radiation and procedure time while improving the needle placement accuracy at the same time [29]. The interventional radiologist can leave the CT room during the acquisition, and therefore is not exposed to ionizing radiation at all. There are also large retrospective studies showing the potential benefits and applications of stereotactic image-guided ablations. While these studies do not show better oncological outcomes when using stereotactic ablation over conventional ablation, they state that the number of patients treated with a curative intent largely increased with the introduction of stereotactic guidance [1, 30, 31]. Furthermore, it has been shown in case-reports that stereotaxy was especially useful in very difficult cases when the tumor would not be reachable with conventional CT guidance [32].

Despite the current evidence showing that stereotactic image-guidance improves ablation needle accuracy and reduces procedure time and radiation dose, the ablation treatment itself has limitations, which are part of the current research—both clinical and engineering research.

4.1 Ablation of larger tumors

One of the short-term improvements of thermal ablations is the reproducible ablation of tumors larger than 3 cm. Current evidence shows that the LTP rate is higher in tumors larger than 3 cm and therefore such tumors are not recommended to treat with ablation [30, 33]. There are studies reporting larger ablation zones when using multiple needles in parallel, which could cover tumors larger than 3 cm [34]. With stereotactic image-guidance, such treatments can be delivered more reproducibly [6]. However, using multiple needles heavily increases the cost for the procedure at some institutions, which can be a major limitation.

4.2 Ablation zone prediction

The planning of the ablation employs the information from the ablation device manufactures' brochures, which presents the expected ablation necrosis that can be obtained for a specific energy delivered. The ablation model presented in the brochures is described as an ellipsoidal or spherical volume, which was obtained from measuring the ablation necrosis in ex-vivo, non-perfused, healthy animal livers. Recent studies have shown that the in-vivo ablation volumes differ significantly from the ex-vivo data, with the in-vivo ablation volumes being much smaller than the ex-vivo data predicts [26, 35]. Future models will be based on retrospective in-vivo data and also take any clinical parameters into account, such as the pathology of the tissue, the patient's clinical background, other treatments being administered (e.g., chemotherapy), and the influence of adjacent blood vessels on the expansion of the ablation volume.

4.3 Quantitative ablation assessment

Recently, there has been a high interest in quantitative ablation assessment to decrease the local tumor progression rates by ensuring complete ablation coverage and sufficient (<5mm) ablation margin using 3D image analysis software [36]. There are several studies that have attempted to describe the ablation success or coverage using numerical metrics derived from 3D tumor and ablation segmentations based on a follow-up scan at 4–8 weeks after ablation [37]. However, a fast intra-operative tool for assessing the ablation outcome would enable an immediate re-ablation and achievement of complete tumor destruction in the same treatment session. The Ablation fit (Ablation-fit, Italy) software is currently the only software available on the market for intra-operative quantitative 3D ablation assessment. However, evidence of the predictive value of intra-operative assessment is still limited as it has been evaluated only at a single center so far and due to the unknown tissue shrinkage after thermal ablation treatment [38].

4.4 Robotics

As in other disciplines in medicine, robotics will also be introduced in interventional oncology on a larger scale. While there are robotic devices available for stereotactic ablations, these are merely motorized arms for alignment. The radiologist still has to be sterile at the CT table and place the needle by hand. However, the future most likely will go toward autonomous robots that plan the trajectory, place the needle, and choose the right amount of energy for ablation. The radiologist might then be able to control the procedure in the control CT room monitoring and approving the robots' decisions [39–41].

5. Conclusion

In conclusion, stereotactic image-guidance provides technical support for accurately planning and placing ablation needles at the desired location and verifying the complete destruction of the tumor. These highly complex systems not only decrease radiation dose, contrast, and needle punctures, but also give a predictable procedure time even in technical challenging cases, which allows to optimally allocate the resources in an interventional radiology suite and most importantly offers the patient a safe and efficient minimally invasive procedure.

Conflict of interest

No conflict of interest.

Author details

Iwan Paolucci[1]*, Raluca-Maria Sandu[1], Pascale Tinguely[2], Corina Kim-Fuchs[2], Martin Maurer[3], Daniel Candinas[2], Stefan Weber[1] and Anja Lachenmayer[2]

1 ARTORG Center for Biomedical Engineering, University of Bern, Bern, Switzerland

2 Department of Visceral Surgery and Medicine, University Hospital of Bern, Bern, Switzerland

3 Department of Diagnostic and Interventional Radiology, University Hospital of Bern, Bern, Switzerland

*Address all correspondence to: iwan.paolucci@artorg.unibe.ch

IntechOpen

© 2019 The Author(s). Licensee IntechOpen. This chapter is distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/3.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

References

[1] Beermann M, Lindeberg J, Engstrand J, Galmén K, Karlgren S, Stillström D, et al. 1000 consecutive ablation sessions in the era of computer assisted image guidance—Lessons learned. European Journal of Radiology Open. 2019;**6**:1-8. Available from: https://www.sciencedirect.com/science/article/pii/S2352047718301072?via%3Dihub [cited March 12, 2019]

[2] Dupré A, Jones RP, Diaz-Nieto R, Fenwick SW, Poston GJ, Malik HZ. Curative-intent treatment of recurrent colorectal liver metastases: A comparison between ablation and resection. European Journal of Surgical Oncology. 2017;**43**(10):1901-1907. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0748798317306467 [cited August 13, 2019]

[3] Leoni S, Piscaglia F, Serio I, Terzi E, Pettinari I, Croci L, et al. Adherence to AASLD guidelines for the treatment of hepatocellular carcinoma in clinical practice: Experience of the Bologna liver oncology group. Digestive and Liver Disease. 2014;**46**(6):549-555. Available from: https://www.sciencedirect.com/science/article/pii/S1590865814002448?via%3Dihub [cited August 13, 2019]

[4] Sastre J, Díaz-Beveridge R, García-Foncillas J, Guardeño R, López C, Pazo R, et al. Clinical guideline SEOM: Hepatocellular carcinoma. Clinical and Translational Oncology. 2015;**17**(12):988-995

[5] Meijerink MR, Puijk RS, van Tilborg AAJM, Henningsen KH, Fernandez LG, Neyt M, et al. Radiofrequency and microwave ablation compared to systemic chemotherapy and to partial hepatectomy in the treatment of colorectal liver metastases: A systematic review and meta-analysis. Cardiovascular and Interventional Radiology. 2018;**41**(8):1189-1204. DOI: 10.1007/s00270-018-1959-3

[6] Bale R, Widmann G, Stoffner DIIR. Stereotaxy: Breaking the limits of current radiofrequency ablation techniques. European Journal of Radiology. 2010;**75**(1):32-36. Available from: https://www.sciencedirect.com/science/article/pii/S0720048X10001774?via%3Dihub [cited July 10, 2019]

[7] Bale R, Schullian P, Eberle G, Putzer D, Zoller H, Schneeberger S, et al. Stereotactic radiofrequency ablation of hepatocellular carcinoma - A histopathological study in explanted livers. Hepatology. 2018:hep.30406. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1002/hep.30406 [cited July 10, 2019]

[8] Wang X, Hu Y, Ren M, Lu X, Lu G, He S. Efficacy and safety of radiofrequency ablation combined with transcatheter arterial chemoembolization for hepatocellular carcinomas compared with radiofrequency ablation alone: A time-to-event meta-analysis. Korean Journal of Radiology;**17**(1):93-102

[9] Tinguely P, Schwalbe M, Fuss T, Guensch DP, Kohler A, Baumgartner I, et al. Multi-operational selective computer-assisted targeting of hepatocellular carcinoma-evaluation of a novel approach for navigated tumor ablation. PLoS One. 2018;**13**(5):e0197914. Available from: http://www.ncbi.nlm.nih.gov/pubmed/29791518 [cited September 04, 2019]

[10] Lencioni R, Crocetti L. Local-regional treatment of hepatocellular carcinoma. Radiology. 2012;**262**(1):43-58. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22190656

[11] Tombesi P, Di Vece F, Bianchi L, Sartori S. Thermal ablation of liver tumours: How the scenario has changed in the last decade. The European Medical Journal. 2018;**6**:88-94

[12] Vogl TJ, Nour-Eldin NEA, Hammerstingl RM, Panahi B, Naguib NNN. Microwave Ablation (MWA): Basics, Technique and Results in Primary and Metastatic Liver Neoplasms - Review Article [Internet]. Vol. 189, RoFo Fortschritte auf dem Gebiet der Rontgenstrahlen und der Bildgebenden Verfahren. 2017. p. 1055-66. Available from: http://www.ncbi.nlm.nih.gov/pubmed/28834968 [cited August 22, 2019]

[13] Potretzke TA, Ziemlewicz TJ, Hinshaw JL, Lubner MG, Wells SA, Brace CL, et al. Microwave versus radiofrequency ablation treatment for hepatocellular carcinoma: A comparison of efficacy at a single center. Journal of Vascular and Interventional Radiology. 2016;**27**(5):631-638. DOI: 10.1016/j.jvir.2016.01.136

[14] Kamal A, Elmoety AAA, Rostom YAM, Shater MS, Lashen SA. Percutaneous radiofrequency versus microwave ablation for management of hepatocellular carcinoma: A randomized controlled trial. The Journal of Gastrointestinal Oncology. 2019;**10**(3):562-571

[15] Facciorusso A, Di Maso M, Muscatiello N. Microwave ablation versus radiofrequency ablation for the treatment of hepatocellular carcinoma: A systematic review and meta-analysis. International Journal of Hyperthermia. 2016;**32**(3):339-344

[16] Ryan MJ, Willatt J, Majdalany BS, Kielar AZ, Chong S, Ruma JA, et al. Ablation techniques for primary and metastatic liver tumors. World Journal of Hepatology. 2016;**8**(3):191-199

[17] Zhu GQ, Sun M, Liao WT, Yu WH, Zhou SL, Zhou ZJ, et al. Comparative efficacy and safety between ablative therapies or surgery for small hepatocellular carcinoma: A network meta-analysis. Expert Review of Gastroenterology and Hepatology. 2018;**12**(9):935-945. Available from: https://www.tandfonline.com/doi/full/10.1080/17474124.2018.1503531 [cited August 22, 2019]

[18] Yu H, Burke CT. Comparison of percutaneous ablation technologies in the treatment of malignant liver tumors. Seminars in Interventional Radiology. 2014;**31**(2):129-137. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25071303 [cited August 19, 2019]

[19] Franz AM, Haidegger T, Birkfellner W, Cleary K, Peters TM, Maier-Hein L. Electromagnetic tracking in medicine—A review of technology, validation, and applications. IEEE Transactions on Medical Imaging. 2014;**33**(8):1702-1725. Available from: http://www.ieee.org/publications_standards/publications/rights/index.html [cited Sepetember 7, 2016]

[20] Oliveira-Santos T, Peterhans M, Hofmann S, Weber S. Passive single marker tracking for organ motion and deformation detection in open liver surgery. Lecture Notes in Computer Science (including Subser Lect Notes Artif Intell Lect Notes Bioinformatics). 2011;6689 LNCS:156-167

[21] Oliveira-Santos T, Klaeser B, Weitzel T, Krause T, Nolte L-P, Peterhans M, et al. A navigation system for percutaneous needle interventions based on PET/CT images: Design, workflow and error analysis of soft tissue and bone punctures. Computer Aided Surgery. 2011;**16**(5):203-219

[22] Toporek G, Wallach D, Weber S, Bale R, Widmann G. Cone-beam computed tomography-guided stereotactic liver punctures: A

phantom study. Cardiovascular and Interventional Radiology. 2013;**36**(6):1629-1637. Available from: http://link.springer.com/10.1007/s00270-013-0635-x [cited July 7, 2016]

[23] Wallach D, Toporek G, Weber S, Bale R, Widmann G. Comparison of freehand-navigated and aiming device-navigated targeting of liver lesions. International Journal of Medical Robotics and Computer Assisted Surgery. 2014;**10**(1):35-43. Available from: http://doi.wiley.com/10.1002/rcs.1505 [cited August 13, 2019]

[24] Beyer LP, Pregler B, Niessen C, Dollinger M, Graf BM, Müller M, et al. Robot-assisted microwave thermoablation of liver tumors: A single-center experience. International Journal of Computer Assisted Radiology and Surgery. 2016;**11**(2):253-259

[25] Engstrand J, Toporek G, Harbut P, Jonas E, Nilsson H, Freedman J. Stereotactic CT-guided percutaneous microwave ablation of liver tumors with the use of high-frequency jet ventilation: An accuracy and procedural safety study. The American Journal of Roentgenology. Jan 2017;**208**(1):193-200. [Internet] Available from: http://www.ajronline.org/doi/10.2214/AJR.15.15803

[26] Ruiter SJS, Heerink WJ, de Jong KP. Liver microwave ablation: A systematic review of various FDA-approved systems. European Radiology. Springer. 2019;**29**:4026-4035. Available from: http://www.ncbi.nlm.nih.gov/pubmed/30506218 [cited August 15, 2019]

[27] Heerink WJ, Solouki AM, Vliegenthart R, Ruiter SJS, Sieders E, Oudkerk M, et al. The relationship between applied energy and ablation zone volume in patients with hepatocellular carcinoma and colorectal liver metastasis. European Radiology. 2018;**28**(8):3228-3236. Available from: http://www.ncbi.nlm.nih.gov/pubmed/29536242 [cited June 6, 2019]

[28] Wang X, Sofocleous CT, Erinjeri JP, Petre EN, Gonen M, Do KG, et al. Margin size is an independent predictor of local tumor progression after ablation of colon cancer liver metastases. Cardiovascular and Interventional Radiology. 2013;**36**(1):166-175. Available from: http://link.springer.com/10.1007/s00270-012-0377-1 [cited August 10, 2019]

[29] Beyer LP, Pregler B, Nießen C, Schicho A, Haimerl M, Jung EM, et al. Stereotactically-navigated percutaneous irreversible electroporation (IRE) compared to conventional IRE: A prospective trial. Peer Journal. 2016;**4**:e2277. Available from: http://www.ncbi.nlm.nih.gov/pubmed/27602266 [cited June 9, 2017]

[30] Tinguely P, Frehner L, Lachenmayer A, Banz V, Weber S, Candinas D, et al. Stereotactic image-guided microwave ablation for malignant liver tumors—A multivariable accuracy and efficacy analysis (In review)

[31] Lachenmayer A, Tinguely P, Maurer M, Frehner L, Knöpfli M, Peterhans M, et al. Stereotactic Image-Guided Microwave Ablation of Hepatocellular Carcinoma using a computer-assisted navigation system. Liver International. 2019:liv.14187. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1111/liv.14187

[32] Fischer T, Lachenmayer A, Maurer MH. CT-guided navigated microwave ablation (MWA) of an unfavorable located breast cancer metastasis in liver segment I. Radiol Case Reports. 2019;**14**(2):146-150. Available from: https://www.sciencedirect.com/science/article/pii/S1930043318301109?via%3Dihub [cited August 13, 2019]

[33] Leung U, Kuk D, D'Angelica MI, Kingham TP, Allen PJ, Dematteo RP, et al. Long-term outcomes following microwave ablation for liver malignancies. The British Journal of Surgery. 2015;**102**(1):85-91. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25296639 [cited August 19, 2019]

[34] Mulier S, Jiang Y, Jamart J, Wang C, Feng Y, Marchal G, et al. Bipolar radiofrequency ablation with 2 × 2 electrodes as a building block for matrix radiofrequency ablation: Ex vivo liver experiments and finite element method modelling. International Journal of Hyperthermia. 2015;**31**(6):649-665

[35] Amabile C, Ahmed M, Solbiati L, Meloni MF, Solbiati M, Cassarino S, et al. Microwave ablation of primary and secondary liver tumours: Ex vivo, in vivo, and clinical characterisation. International Journal of Hyperthermia. 2017;**33**(1):34-42. Available from: https://www.tandfonline.com/doi/full/10.1080/02656736.2016.1196830 [cited August 19, 2019]

[36] Hocquelet A, Trillaud H, Frulio N, Papadopoulos P, Balageas P, Salut C, et al. Three-dimensional measurement of hepatocellular carcinoma ablation zones and margins for predicting local tumor progression. Journal of Vascular and Interventional Radiology. 2016;**27**(7):1038-1045.e2. Available from: https://www.sciencedirect.com/science/article/pii/S1051044316003821?via%3Dihub [cited August 19, 2019]

[37] Kaye EA, Cornelis FH, Petre EN, Tyagi N, Shady W, Shi W, et al. Volumetric 3D assessment of ablation zones after thermal ablation of colorectal liver metastases to improve prediction of local tumor progression. European Radiology. 2019;**29**(5):2698-2705. Available from: http://link.springer.com/10.1007/s00330-018-5809-0 [cited August 19, 2019]

[38] Solbiati M, Muglia R, Goldberg SN, Ierace T, Rotilio A, Passera KM, et al. A novel software platform for volumetric assessment of ablation completeness. International Journal of Hyperthermia. 2019;**36**(1):337-343. Available from: https://www.tandfonline.com/doi/full/10.1080/02656736.2019.1569267 [cited August 19, 2019]

[39] Ben-David E, Shochat M, Roth I, Nissenbaum I, Sosna J, Goldberg SN. Evaluation of a CT-guided robotic system for precise percutaneous needle insertion. Journal of Vascular and Interventional Radiology. 2018;**29**(10):1440-1446

[40] Hiraki T, Matsuno T, Kamegawa T, Komaki T, Sakurai J, Matsuura R, et al. Robotic insertion of various ablation needles under computed tomography guidance: Accuracy in animal experiments. European Journal of Radiology. 2018;**105**:162-167

[41] Hiraki T, Kamegawa T, Matsuno T, Komaki T, Sakurai J, Kanazawa S. Zerobot®: A remote-controlled robot for needle insertion in CT-guided interventional radiology developed at Okayama University. Acta Medica Okayama. 2018;**72**(6):539-546. Available from: http://www.ncbi.nlm.nih.gov/pubmed/30573907 [cited August 19, 2019]