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# 1000 consecutive ablation sessions in the era of computer assisted image guidance – Lessons learned☆

Marie Beermann[a], Johan Lindeberg[a], Jennie Engstrand[b], Karolina Galmén[c], Silja Karlgren[b], David Stillström[b], Henrik Nilsson[b], Piotr Harbut[c], Jacob Freedman[b,*]

[a] Dept of Radiology, Danderyd University Hospital, Stockholm, Sweden
[b] Dept of Surgery and Urology, Danderyd University Hospital, Stockholm, Sweden
[c] Dept of Anaesthesiology, Danderyd University Hospital, Stockholm, Sweden

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ABSTRACT

*Background:* Ablation therapies for tumours are becoming more used as ablation modalities evolve and targeting solutions are getting better. There is an increasing body of long-term results challenging resection and proving lower morbidities and costs. The aim of this paper is to share the experiences from a high-volume centre in introducing computer assisted targeting solutions and efficient ablation modalities like microwave generators and irreversible electroporation.

*Material and methods:* One thousand consecutive treatments in one high-volume centre were evaluated retrospectively from prospectively collected data.

*Results:* The purpose of this paper is to present the benefits of going into computer assisted targeting techniques and microwave technology; pitfalls and overview of outcomes. The main target organ was the liver and the main indications were ablation of hepatocellular carcinomas and colorectal liver metastases. With the assistance of computer assisted targeting the local recurrence rate within 6 months has dropped from 30 to near 10%. The survival of patients with hepatocellular carcinoma and colorectal liver metastases is not worse if the tumour can be retreated after a local recurrence. Multiple colorectal liver metastases can be treated successfully.

*Discussion:* The incorporation of computer assisted targeting technologies for ultrasound-, ct guided- and laparoscopic tumour ablation has been very successful and without a noticeable learning curve. The same is true for switching from radiofrequency energies to microwave generators and irreversible electroporation.

*Conclusion:* It is well worthwhile upgrading ablation and targeting technologies to achieve excellent and reproducible results and minimizing operator dependency.

## 1. Introduction

Local ablative treatment of soft tissue tumours has developed over the last decades from being used as a palliative treatment to being accepted as a curative treatment. The indications are still developing but generally resective surgery is often regarded as the first choice [1,2].

The benefits of ablative treatment is the possibility of a minimal invasive approach with minimal collateral damage to the target organ. Targeting is typically achieved with a percutaneous approach using ultrasound, computed tomography or magnetic resonance imaging, with or without computer assisted guidance. Laparoscopic or open approaches are sometimes safer in cases where adjacent organs are in close proximity to the targeted tumour. Organs that are typically targeted are liver, kidneys, pancreas and lungs but any tumour that can be targeted without causing harm to adjacent organs can be treated, thus breasts, prostate, bone, uterus, spleen and lymphoid tissues have been treated.

The complication rate after ablative treatment is in the range of 16–25% of what is seen after open surgeries, where typically around 40% get adverse events. Serious complications requiring any kind of reintervention is typically around 10% for open liver resections and around 2% after percutaneous ablations [3]. Another advantage is

*Abbreviations:* SBRT, stereotactic body radiation therapy; HIFU, high intensity focused ultrasound; RFA, radio-frequency ablation; MWA, microwave ablation; IRE, irreversible electroporation; TAE, TACE, trans-arterial embolization or chemo-embolization; CAS, computer assisted surgery; HFJV, high frequency jet ventilation; TIVA, total intravenous anaesthesia

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* Corresponding author at: Dept of Surgery and Urology, Danderyd University Hospital, 18288, Stockholm, Sweden.
*E-mail address:* jacob.freedman@ki.se (J. Freedman).

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shorter length of stay where an ablation can be performed as an outpatient procedure or with a single day of care as compared to liver resected patients who are typically in hospital for 7–10 days [4].

Ablation modalities range from non-invasive external focused radiation (SBRT) and high intensity focused ultrasound (HIFU) to invasive freezing or heating of tumours with laser energy, radio-frequency energy (RFA) or microwaves (MWA). Tumours can also be destroyed with intense electrical pulses as in irreversible electroporation (IRE), or with direct injection of toxic agents, such as concentrated ethanol or acetic acid, or with indirect injection through vessels with ischemia-causing embolizing agents with or without chemotherapeutic drugs or radiating isotopes (TAE, TACE). So far, thermal treatment has been the most effective modality with MWA outperforming RFA in most respects [5,6]. When thermal ablation is inadvisable, like in the liver hilum or in the pancreas, IRE is a promising alternative.

This paper presents the experiences of a high-volume centre using microwaves as the primary energy source and IRE as an alternative where thermoablation is ill advised, during a period of time when computer assisted planning and targeting has been introduced. The aim is to help others in making the transition into an optimized centre for local ablative therapies.

## 2. Methods

Prospective data was collected for all patients undergoing ablative treatment since the introduction of the microwave ablation technique in 2010 until the thousand treatment in November 2017. Follow-up data was collected until September 15, 2018 with complete follow-up on mortality except for one foreign national. Data on choice of energy and brand was recorded as well as procedural data, complications within 30 days, recurrences, retreatments and survival. All patients were followed for at least six months. Technical success was evaluated immediately after ablation when possible, otherwise within one day. Local recurrence was defined as a new tumour within 1 cm of the ablation zone within 6 months of the ablative treatment.

Microwave sources used were Acculis (Angiodynamics, Latham, NY USA), Amica (HS Hospital service S.P.A, Roma, Italy) and Emprint (Covidien, Minneapolis, USA) systems. IRE was done using the Nanoknife system (Angiodynamics, Latham NY, USA). Computer tomography targeting was enhanced with the CAS-one system (Cascination AG, Bern, Switzerland), a system that uses six retro-reflective small spheres that are glued to the skin in the area of interest, before acquisition of CT images, where these spheres are recognized by a stereotactic camera that also guides the ablation device to a definable point within the body from any point on the skin using a rigid aiming device [10]. Fused ultrasound was made with the Toshiba Aplio 500 and LOGIQ E9 systems. Four skilled radiologists performed the ultrasound guided interventions. The CT-guided interventions included an additional six surgeons.

The retrospective study was approved by the regional ethics committee.

### 2.1. Statistical analysis

Descriptive statistics was used to describe baseline characteristics with medians for non-normally distributed data and categorical variables were expressed as total and frequencies. Overall survival was illustrated using Kaplan-Meier curves and differences in survival analyzed with log-rank test.

## 3. Results

Over all demographic data is presented in Table 1. All liver ablations in the region were centralised in 2012 (population 2.7 million) and since the practice has grown and also acted as a national reference centre for difficult and special cases. Details on treatments are shown in Table 2, the most common patient having a hepatocellular carcinoma, closely followed by colorectal liver metastases. The by far most common treatment modality was microwave technology and most tumours were targeted using computer assisted techniques.

**Table 1**
Presentation of over all demographics. MDT = multi disciplinary team conference.

| | n (%) |
|---|---|
| Gender | |
| Female entries | 303 (30%) |
| Female, unique individuals | 196 (32%) |
| Male entries | 697 (70%) |
| Male, unique individuals | 409 (68%) |
| Age | |
| < 50 | 71 (7%) |
| 50-65 | 313 (31%) |
| 65-80 | 494 (49%) |
| > 80 | 119 (12%) |
| missing data | 3 |
| Year | |
| 2010 | 7 |
| 2011 | 22 |
| 2012 | 58 |
| 2013 | 76 |
| 2014 | 160 |
| 2015 | 197 |
| 2016 | 237 |
| 2017 | 243 |
| Time from diagnosis to ablation, median (90% range) | 55 days (17-291) |
| Time from MDT to ablation median (90% range) | 27 days (12-89) |

**Table 2**
Tumours treated and modalities used. HCC = hepatocellular carcinoma, CRLM = colorectal liver metastases, NET = neuroendocrine tumours, RCC = renal cell carcinoma, MWA = microwave ablation, RFA = radiofrequency ablation, IRE = irreversible electroporation, PEIT = percutaneous ethanol injection therapy. CAS = computer assisted surgery.

| | Number of treatments | Number of tumours |
|---|---|---|
| **Indications** | | |
| HCC | 475 | 843 |
| CRLM | 341 | 1244 |
| NET | 43 | 193 |
| RCC | 93 | 98 |
| other | 48 | 117 |
| **Location** | | |
| Liver | 891 | 2382 |
| Kidney | 93 | 98 |
| Lung | 14 | 32 |
| Pancreas | 4 | 4 |
| **Ablation modality** | | |
| MWA | 881 | 2270 |
| IRE | 64 | 74 |
| RF | 60 | 62 |
| PEIT | 17 | 40 |
| **Targeting** | | |
| Open surgery | 28 | 45 |
| Laparoscopic | 28 | 32 |
| Percutaneous ultrasound | 94 | 145 |
| Computer Tomography | 5 | 6 |
| Open CAS | 29 | 281 |
| Laparoscopic CAS | 79 | 438 |
| Percutaneous CAS | 374 | 787 |
| Percutaneous fused ultrasound | 337 | 583 |

### 3.1. Targeting

#### 3.1.1. Ultrasound

Traditionally, ultrasound has often been used for lesion targeting, as it has obvious advantages such as availability and visual control of applicator placement. However, many lesions are difficult to detect by ultrasound alone, which will result in incomplete ablations or no ablation at all in cases where the target cannot be found. This is especially true for HCC in cirrhotic livers.

With a percutaneous approach, it was soon evident that the local recurrence rate, defined as a new detection of a tumour within six months and within 10 mm from the ablation zone to the centre of the recurrence, was unacceptably high at 30%. With an open approach, often simultaneous with a colonic resection, the hit-rate was much better with a per lesion recurrence rate of 5%. To increase the efficacy of the percutaneous approach, targeting systems with ultrasound using CT or MRI fusion and a computerized targeting system for CT-guided procedures were incorporated and further developed. With the introduction of these techniques, the local recurrence rate per lesion for a first treatment has dropped to 13% (29/233) for ultrasound with fusion and 9% (18/217) for CT with computer assisted targeting, p = 0199. There is no clear improvement over time so the techniques have been found to be easy to assimilate.

#### 3.1.2. Fused ultrasound

Many modern ultrasound systems have the possibility of image fusion between live ultrasound and a previous scan (CT, MRI or ultrasound). There are studies indicating that this method increases the conspicuity of liver lesions in US-guided MWA [7].

As almost all patients accepted for liver ablation in the present material have had a recent CT or MRI of the tumour of interest, fusion is used as a standard technique for improving tumor detection and targeting.

Easily identifiable liver vessels are used for reliable fusion thus allowing for high precision applicator placement regardless of tumor conspicuity. As fusion makes sure that US tumour detection is focused within the area of interest, it is often possible to detect even almost invisible lesions and with the use of contrast enhanced ultrasound (CEUS) accuracy can be improved even more (Fig. 1).

In the kidneys, where manual fusion is more difficult due to the lack of obvious landmarks, there is the possibility of using an auto tracking device (for the LOGIQ E9). As the tracker needs to be attached to the patient in the exact same position during both the CT and the subsequent ultrasound in order to work, this regime requires a dedicated CT scanner available during ultrasound guided ablations. In our experience, the auto tracker is not as accurate as meticulous manual fusion, but even so it is still useful and timesaving in selected patients.

#### 3.1.3. Computer assisted CT targeting

With computer assisted CT-targeting using the CAS-one system (Cascination AG, Bern, Switzerland), it was immediately evident that problems with shifts in the position of the target organ had to be minimized as the tumour is targeted after the acquisition of the relevant images. Thus a very good accuracy in 3d space can be had but measures has to be made to inhibit shifts of the targeted tumour. This can happen with normal respiration where the liver can be displaced with up to 30 mm with each breath. The solution to this problem was the use of high-frequency jet ventilation where respiratory movement of abdominal organs are minimized to 2–3 mm [8,9]. Other sources of organ displacement over time is the formation of lung atelectases, pneumothorax or bleeding under the liver capsule when targeting more than one tumour, oedema around larger ablated tumours and also varying muscular relaxation levels during the course of the anaesthesia.

Free-hand applicator insertion was discontinued early on because of difficulties in keeping a straight trajectory and applicator guides were introduced and developed. The first generation typically gave a lateral positioning error of around 4 mm on average [10]. With the second generation of aiming device the error is now on average less than 3 mm (Fig. 2). It is advisable to always do a control scan with the applicator in place before delivering energy.

When treating multiple lesions it is paramount to do these in a sequence that minimize possible target organ movement so that lesions in need of high accuracy are done first and targeting risking a pneumothorax, for example, are done last. When in doubt one can do a second contrast study or continue the treatment in a new session.

Lung ablations with CAS-one and CT is an attractive choice for lung treatments as the antenna placement is quick and accurate which could reduce the risk for postoperative pneumothorax [9]. Ten interventionists (radiologists and surgeons) performed the CT guided interventions without any difference in ablation site recurrence rate,

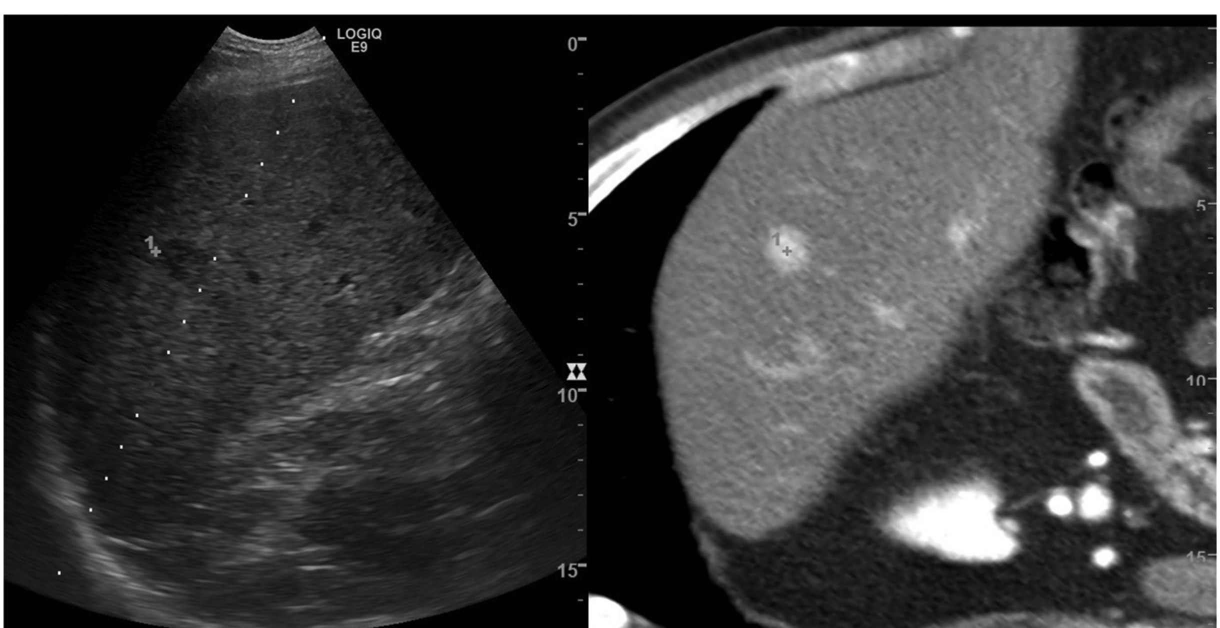


**Fig. 1.** Liver tumour with arterial loading on computed tomography fused with live ultrasound for easier targeting.

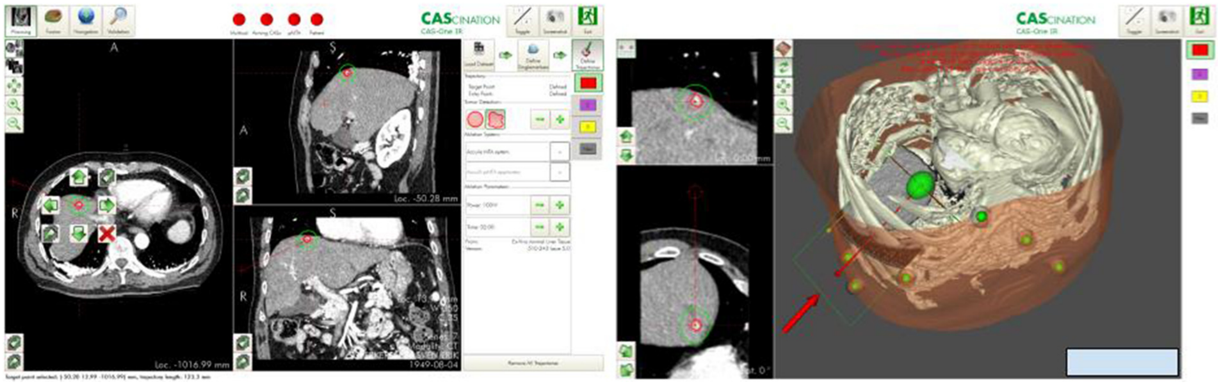

**Fig. 2.** Image of screen dumps from an intervention with a tumour in a hard to reach area on the dome of the liver in the border between segment 4a and 8. The system gives reconstructions of all standard planes and also the planned needle plane as well as a 3d reconstruction of the area of interest with glued on reflective skin markers for optical tracking in bright green on the skin, the tumour segmented in red and the planned ablation volume lit up in green (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article).

highlighting the ease of navigation using the system.

#### 3.1.4. Laparoscopic approach

Laparoscopic targeting is sometimes very easy with readily visible tumours, but very difficult when out of sight. We have found it useful to use the CAS-one liver surgery software to help in determining depth of insertion and to approximate the energy needed. It is also very useful for keeping track of the lesions that have been ablated when doing multiple ablations [11,12]. It is also prudent to use laparoscopic ultrasound to ascertain accurate applicator placement. The CAS-one system permits efficient use of out of plane applicator insertions making the ultrasound probes applicator-guide, which is often very hard to use in a laparoscopic setting, superfluous. Still, it is very difficult to get good accuracy in deeper parts of segments 6, 7 and 8. It is often easy to reach targets in segment 1 and those that are near other organs making the percutaneous approach difficult, for example near the stomach on the dorsal aspect of the lateral segment, near the gallbladder (that can laparoscopically be moved or removed), near the right colonic flexure, and on the ventral aspects of segments 2,3,4,5,6 and 8. For targeting of the pancreas we have found the laparoscopic approach to be working well [13]. It allows mobilization of the stomach and safe introducing of IRE electrodes into the ventral aspect of the pancreas using CAS-one with 3d imaging to ensure good electrode accuracy. Previous open surgery is not a contra-indication as it is often possible to reach the liver surface, however a previous open liver resection can be very difficult to deal with laparoscopically a second time because of adhesions and scar tissue.

#### 3.1.5. Open approach

Open surgery allows for the liver to be properly mobilised and with the help of vision, tactile senses ultrasound and 3d imaging (CAS-one) most lesions can be targeted safely. However, open surgery will reduce the benefits of ablation as it is no longer a minimally invasive approach. In a small minority of patients with multiple lesions, an open approach may however be the best choice.

Fused ultrasound is chosen for the third of cases with readily reachable targets since access to the CT-suite is limited. Computed tomography with computer assisted targeting is used for half of the patients with more difficult-to-reach lesions and a laparoscopic approach for the rest when there are risks for harming adjacent organs and for lesions in segment 1 of the liver.

### 3.2. Energies

#### 3.2.1. Microwaves

The default energy source is microwaves. Different 2.45 GHz systems are used interchangeably. It is important to recognize that manufacturers ablation volume guides overestimates the ablation radius by up to 10 mm except for the Emprint system that delivers more consistent ablation volumes, but somewhat slower. The switch to microwaves from RFA was done because of its more predictable ablation volumes, larger volumes, quicker application of energy and less risks of heat-sink problems thereby potentially improving outcome and minimizing incomplete ablations. For CT-guided ablations it is helpful to have stiff antennae to reduce targeting errors caused by bending of the antenna shaft.

#### 3.2.2. Radiofrequency

The radiofrequency equipment was kept for renal ablations where it is sometimes regarded as safer to use since it is a less potent energy source. With time, this indication is no longer used.

#### 3.2.3. Irreversible electroporation

The NanoKnife (Angiodynamics, NY, USA), system is used for electroporation. The technique is well described elsewhere [14] and is gaining in clinical use for the treatment of unresectable smaller tumours adjacent to heat sensitive structures, like bile ducts and nerves. The current available system depends on multiple electrodes around, and sometimes within, the tumour. The electrodes need to be parallel and 15–25 mm. apart.

Going from ablation with single applicator to ablation with multiple electrodes and the demand of parallelity is a challenge. It is much more time consuming as electrodes tend to get in the way and ribs and adjoining organs as well, when doing it percutaneously. The need for preoperative planning is greater. It also takes some practise to get familiar with the NanoKnife system that lacks somewhat in user friendliness.

Together with CAScination AG in Bern software for multiple electrode placement with the CAS-one targeting device has been developed. This has been very helpful in many ways; the collaborative planning of the procedure is much easier when using the images from the CT scanner compared to when using ultrasound targeting. A robust and exact electrode guide was developed for easy percutaneous placement of multiple electrodes. The CAS-one system is the electrode placement tool of choice.

### 3.3. Liver

#### 3.3.1. Complications

Ablative therapy has a documented lower complication rate than resection [15]. The present material has similar results with four deaths (0,4%) noted and 9 complications requiring intervention in general or

**Table 3**
Distribution of complications according to the Clavien-Dindo [16] scale, all treatments included.

| Clavien-Dindo | n |
|---|---|
| 0 | 818 |
| 1 | 68 |
| 2 | 78 |
| 3a | 23 |
| 3b | 7 |
| 4a | 1 |
| 4b | 1 |
| 5 | 4 |

regional anaesthesia (0,9%), see Table 3.

The four deaths were one immediate postoperative hemorrhage after a laparoscopic ablation of a HCC in segment 4a in a cirrhotic liver. Despite an emergency laparotomy no bleeding point could be located and the patient did not recover after the hypovolemic shock. One patient developed kidney failure after laparoscopic ablation of twenty colorectal liver metastases. Multiorgan failure followed and the course could not be reversed. One patient with cirrhosis went in to terminal liver failure and the last died of a cardiac infarction three weeks after ablation of colorectal metastases. Initially there was a normal early post-operative course and early discharge. He returned after three weeks with a small perforation of a loop of ileum that was close to the ablated part of the liver in segment 6. The perforation was repaired with open surgery with a normal postoperative course until sudden cardiac shock on postoperative day three.

The complications requiring intervention in anaesthesia (3b + 4) were three patients with bleeding complications, one patient with a partial liver necrosis with sepsis, one bile leak with sepsis, one with sepsis, one patient with pleural effusion, one with acute liver failure and perforation of intestine and one with a wound dehiscence after the colonic part of a simultaneous operation of primary and liver metastases

Patients are typically discharged after an overnight stay, but over time the procedure is done more frequently as day-care surgery, see Fig. 3. The longer hospital stays are usually associated with simultaneous colon resections. These numbers are lower than previously reported [17,18] but these differences may be cultural as length of hospital stay depends on a multitude of factors. Low molecular weight heparin is administered subcutaneously for ten days and pain relief is prescribed as needed, most often not at all.

### 3.3.2. HCC

In the first thousand treatments, 310 patients had a first treatment for HCC, 118 of these (38%) had a further ablation, 55 (18%) had a third ablation, 25 (8%) had a fourth and 6 (2%) had a fifth ablative liver

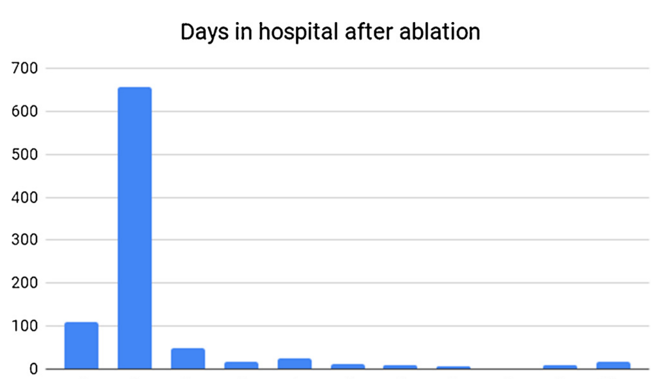


**Fig. 3.** Frequency distribution of number of days in hospital for all patients.

intervention. The patients with cirrhosis grade Child-Pugh A had a better survival than the grade B group (p = 003) Fig. 4A. Results are similar to what has been reported from China [19] and Europe [20].

For patients that had an initial incomplete ablation, a second completing ablation was performed whenever possible and the survival was not in any way worse because of the initial inadequate technical success, se Fig. 4B, which is well in line with previous publications [21] but in contrast with the worse survival noted by Facciorusso et al. [22]. For HCC it is important to note that the reported survival is over all and not cancer specific, as for many patients the cirrhosis is significant risk factor in itself, with or without recurrent tumour status. An in depth analysis of outcomes is being performed but outside the scope of this report.

### 3.3.3. Colorectal metastases

Two hundred and twelve patients had a first ablative treatment for colorectal liver metastases after selection at the regional liver multidisciplinary team conference. Most for reasons where resection was not an option, but to a lesser extent also for inclusion in an ongoing study of microwave ablation versus resection for colorectal liver metastases. The difference in survival did not reach a statistical significance when stratified for the number of tumours treated, Fig. 4D. Five-year survival is somewhat lower than what has been reported for resections, which is probably due to selection bias, but better than what has previously been reported for ablative treatment of colorectal liver metastases [15]. As for the primary hepatocellular carcinomas, an initial incomplete ablation did not adversely affect survival, Fig. 4C.

Eighty-five patients had a second ablation (40%). 33 had a third ablation (16%) and 13 had four or more procedures. The average number of tumours per treatment session was 3.6.

Further investigations are being completed with propensity score comparisons between resections and ablations as well as a prospective multinational multicentre study (MAVERRIC, see clinicaltrials.gov) where patients with 1–5 liver metastases not larger than 3 cm amenable to both resection and computer assisted CT-targeted microwave ablation, are compared regarding survival.

### 3.3.4. Neuroendocrine metastases

Patients were treated mainly as a debulking strategy for liver metastases causing hormonal symptoms or where some metastases showed an increasing activity on radiological examination. Twenty nine patients have been treated 43 times for 193 metastases. Four patients have died with the longest follow-up of 8 years since first treatment.

### 3.3.5. Other

Small numbers of patients have been treated for liver metastases of other primary tumours like cholangiocarcinoma, breast cancer, melanoma and kidney cancer. This only after decision at the tumour board and for specific reasons, as evidence of a survival benefit with these diagnoses is lacking.

## 3.4. Kidney

Ablation is gaining acceptance for the treatment for small kidney tumors (up to 3 cm in size) in selected patients, with survival comparable to partial nephrectomy [23,24].

With the development of pulsated microwave deposition allowing for a more controlled and spherical ablation zone, MWA has replaced RFA in our clinical practice. As most kidney tumours are visible with ultrasound, it is the method of choice for needle placement (with or without fusion, see above). However, these tumors are often very dense in composition, and with the kidney being a movable organ surrounded by fat which reduces US needle detectability, it is advisable to performing the ablation in the CT suite allowing for a control scan of needle position before deploying energy.

As in the liver, tumors close to heat sensitive structures might not be

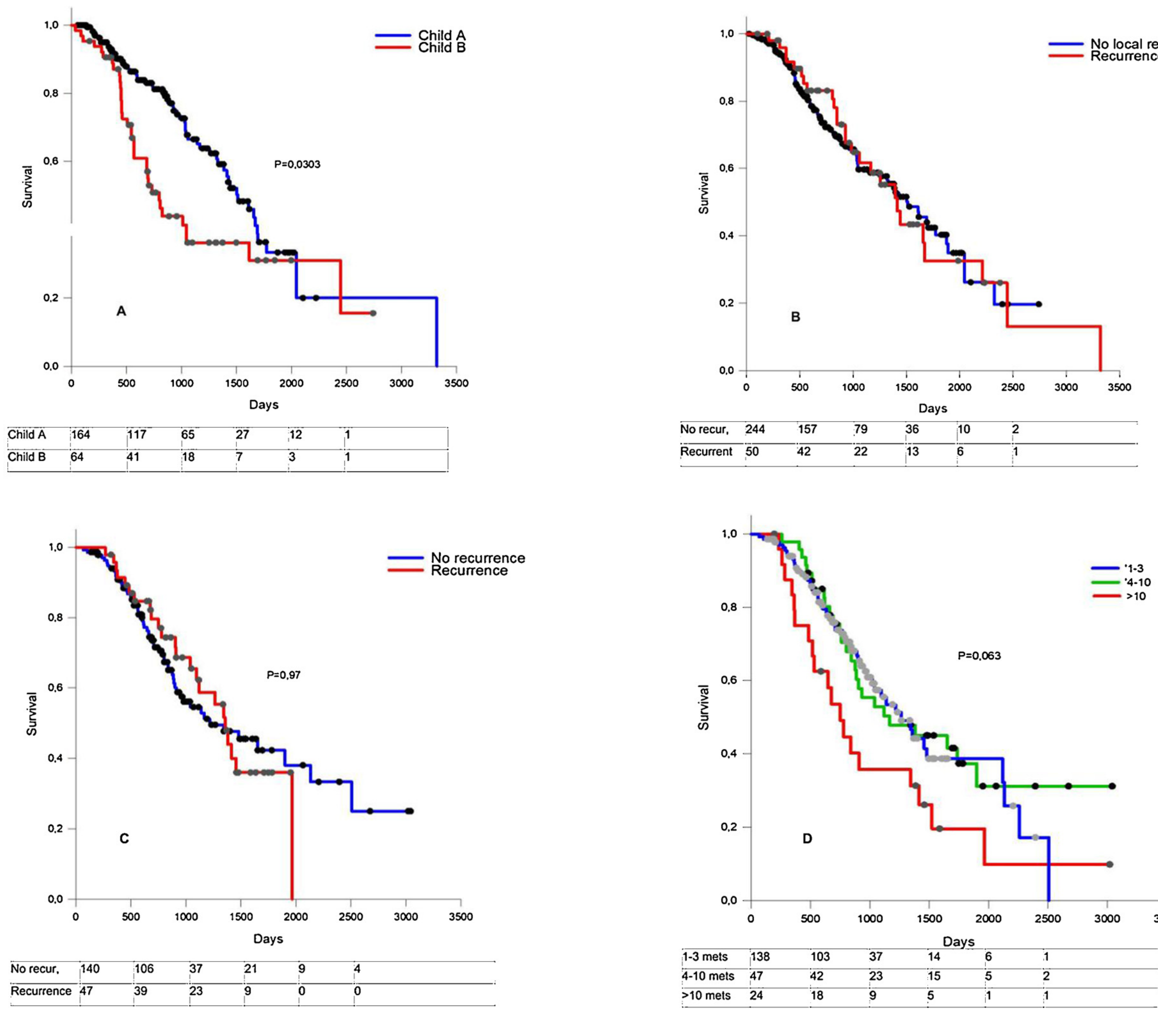


**Fig. 4.** (A).Survival after a first liver ablation for hepatocellular carcinoma in patients with cirrhosis grade A and B. Table showing numbers remaining in the survival analysis. (B).Survival after retreating local recurrent hepatocellular carcinoma within 6 months from first treatment. (C).Survival after retreating local recurrent colorectal liver metastasis. (D).Survival after ablation of colorectal liver metastases stratified by number of tumours treated.

suitable for thermal ablation. However, in the kidney there is the possibility of applying cooling through a catheter in the ureter, and thus allowing treatment of more central lesions close to the collecting system or the ureteropelvic junction. Bowel in close proximity to the tumor might also cause problems with a percutaneous approach, but this can be overcome by hydrodissection of the structure at risk. As with all treatment options for these small kidney tumours, survival is excellent and during the observation period only three of the 93 patients have died.

### 3.5. Lung

When lung tumours cannot be resected, for various reasons, ablative treatment can be an option. Traditionally stereotactic body radiation therapy (SBRT) and radiofrequency technology has been reported with good results [25–27]. Also cryotherapy has been an option. Irreversible electroporation has not quite lived up to expectations but this is logical since currents are limited in the air rich environment [28]. To effectively treat a tumour the electrodes would have to be inside the tumour and not around it, as is the preferred technique for liver or pancreas. Having ablation electrodes pass through tumours could increase the risk for seeding. In the present material microwaves have been used to deliver thermal energy during general anaesthesia with high-frequency jet ventilation. Microwaves are transmitted well through air and give a quick and predictable ablation zone. Stereotactic targeting is easy and since there is no need for intravenous contrast medium, repeat image acquisition is possible when ablating multiple tumours. The risk for pneumothorax is around 25% and when this happens, the air can typically be evacuated by aspiration through a intrapleurally inserted subclavian access catheter, with the option of a Bülau drain if the pneumothorax recurs.

We have previously published two case reports where microwave ablation of lung metastases were coincidental with immunotherapy (one child had bone marrow transplantation and an adult were started on PD-1 inhibition) were synergistic effects and possible abscopal effects were noted [9,28,29].

The present series includes 13 patients with 15 sessions for 34 tumours and is small in comparison with previously reported series [30–32]. Three patients had evacuation of a pneumothorax. All were admitted overnight and could be discharged the next day with minimal discomfort. One patient returned with pneumothorax after six days and received a chest drain with suction for four days.

### 3.6. Pancreas

Four patients with locally advanced pancreatic cancer have been treated laparoscopically. Images from preoperative CT scans were processed by MEVIS and downloaded to the Cascination devise. The electrodes were placed through the abdominal wall and guided with CAScination and laparoscopic ultrasound. This method has been described in a previous publication by our group [13].

IRE in the pancreas is painful and all patients were given an epidural catheter for per- and postoperative pain relief. Pancreatitis is a well-known risk and one of our patients had a severe pancreatitis with a rupture of the main pancreatic duct with development of a pancreatic cyst that gave her problems for almost three months. Another patient presented with abdominal pain and neurological symptoms two days after surgery. CT scans showed duodenal perforation with intra-abdominal abscess and intra-spinal gas. Spinal tap showed bacterial and fungal infection. The duodenal perforation was treated with a covered duodenal stent. This patient had a large tumour and nine electrodes were used to treat it.

The published data from IRE of locally advanced pancreatic cancers are all case series. No randomized clinical trial has been published. We have embarked on such a trial.

### 3.7. Evaluation of ablations

Post ablation imaging is crucial for evaluation of treatment as well as early detection of recurrence. It can be done with different modalities, and it is important for every radiologist to be familiar with normal as well as pathological appearances.

In the liver, the ablation zone should cover the treated tumor with a margin of at least 5–10 mm, analogous to the tumor free resection margin after hepatic surgical resection. Sometimes the ablation and subsequent scarring will alter the liver anatomy, and make comparisons with pre-ablation imaging difficult. This can be overcome by comparing vessels adjacent to the original tumor on pre- and post-op imaging. In the case of uncertainty, the next follow up scan should be brought forward in order to detect possible residual tumor for re ablation. Other things to consider in the liver are vascular changes caused by ablation, which might mimic the hypervascularity of HCC. Vascular changes can be due to hyperemia caused by inflammatory response induced by the ablation and will disappear over time [33]. Ablation can also damage small vessels or create arteriovenous fistulas, which can cause vascular changes especially in the arterial phase.

Many patients with metastatic liver disease have ablated several lesions, and especially on CT new metastasis might be almost impossible to differ from old ablation zones. Here previous imaging is necessary for comparison. At first, recurrence might just be visible as a small irregularity of the ablation zone, but any increase in size should raise the suspicion of local recurrence as ablation zones do not grow. MRI is more sensitive in detecting residual disease than CT (89% vs 44%) [33] and should be used for follow up of patients with CRM when possible.

In the case of IRE, the appearance on follow-up is more varied than after thermal ablation. A persisting rim of increased contrast enhancement can cause diagnostic difficulties especially in HCC patients [34]. However, the ablation zone will shrink over time and might disappear completely as the liver regenerates.

For the follow up of kidney tumors, multiphase CT is the method of choice (native, arterial- and late phase). In the absence of contrast enhancement the tumor is radically treated, while enhancing lesions in the vicinity of the ablation zone mean residual tumor or recurrence. However, on CT there might be a pseudo enhancement [35] difficult to differ from viable tumor, and in those cases CEUS is an excellent complement.

Ablation zones in the lung is seen as atelectasis infiltrates that might be difficult to differ from original tumor, at least on early follow up [36]. Over time, however, the infiltrate will shrink, and as in other organs growth and/or contrast enhancement is sign of recurrence.

### 3.8. High-frequency jet ventilation

High frequency jet ventilation (HFJV) is a technique for artificial ventilation of the lungs with sub-dead space tidal volumes, delivered using supra-physiological frequencies. The method has been known and used since the 1960′s, mostly in ear-nose and throat surgery (ENT) anesthesia in cases where availability of the surgical field is in conflict with the priorities of airway management. A growing interest for this method of ventilation has been observed over the recent years, especially in minimally invasive procedures relying on radiological data, extracorporeal shockwave lithotripsy (ESWL) [37] and catheter procedures for atrial fibrillation treatment [38]. The use of HFJV markedly reduces the amplitude of respiratory movements and ensures near static conditions of upper-abdominal and intrathoracic organs, thus enhancing surgical precision [39]. Biro et al showed that breathing-related liver motion decreased from 20 mm to 5 mm using HFJV compared to conventional ventilation [40].

Since HFJV is an open system, a total intravenous anaesthesia (TIVA) is preferred. In our institution, we use propofol, remifentanil and rocuronium for muscle relaxation. Carbon dioxide ($CO_2$) retention and build-up of an occult post-expiratory pressure end pressure (PEEP) are the most known side effects of the use of HFJV. To minimize these risks we use an endotracheal tube one size greater than would be used otherwise, that is size 8 for woman and size 9 for men. The HFJV ventilator we use (Monsoon Jet Ventilator, Acutronic, Switzerland) is equipped with an end-tidal $CO_2$ sampling module. The $EtCO_2$ measurements are done by pausing the HFJV either on demand, or automatically, so that the jet-ventilator samples gas during a series of five insufflations. The values achieved this way, compares reasonably to the arterial blood gases. Furthermore, the $CO_2$ sampling procedure can influence the surgical precision, similar to conventional lung ventilation. Therefore continuous transcutaneous carbon dioxide monitoring ($tcCO_2$) is strongly recommended. The accuracy of $tcCO_2$ monitoring is independent from the mode of lung ventilation and does not interfere with the surgical procedure. In our practice we use a TCM5 monitor (Radiometer, Denmark).

Even though we manage the patients' airways with the endotracheal tube and use the ventilators built-in humidification as well as safety alarm features, the use of HFJV still, theoretically, introduces some risk. However, in our experience, risk factors like barotrauma and tracheal mucosal necrosis due to dehydration seems to be of historical rather than clinical importance.

HFJV can be used safely in most patients and the equipment is easy to operate by the anesthesia staff after a short introduction.

At the beginning, our experience with HFJV was limited. Establishing the optimal settings, choice of anesthesia and airway management was a matter of experimentation and collaboration between surgeons and anesthesiologists. After a while, best practices were established based on demands of the modern surgical environment as well as to ensure the patients' safety.

A series of clinical trials is currently taking place with focus on respiratory implications such as atelectasis formation, circulatory profile in high risk patients as well as $CO_2$ control during various abdominal surgical procedures when using HFJV.

### 3.9. Follow-up protocol

At least one third of the patients ablated for liver tumors will develop new lesions due to their underlying diagnosis (cirrhosis or metastatic disease) and may thus need further treatment. If recurrence free, the patients with CRM are followed every third month for 6 months and the patients with HCC every third month for 12 months. In our experience, multiphase CT with a high dose of iodine and high radiation is a good option for patients already treated for HCC. Native phase is not needed, but a late arterial phase as well as portal venous phase and late phase is mandatory. In the case of equivocal CT findings, a complementary MRI is needed (preferably with Multihance). For metastatic disease, MRI with Primovist is the method of choice as discussed above, and CT is used only for patients not tolerating MRI.

After this initial time of follow-up the patients are referred back to their colorectal surgeons, oncologists or hepatologists for long-term follow-up.

All treatments are prospectively entered into the swedish national liver registry (Sweliv) which permits long term follow-up and comparisons beteende different treatment modalities. An effort that is recommended for all centres with ambitions in advancing minimally invasive ablative tumour treatment.

## 4. Future perspectives

With the aid of effective energy delivery in the form of microwaves and irreversible electroporation, and with the assistance of navigated targeting, ablative therapy of soft tissue tumours has come of age and within reach of all interventionists. Local ablative treatments may also in the near future be an integral part of boosted immunotherapy regime.

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