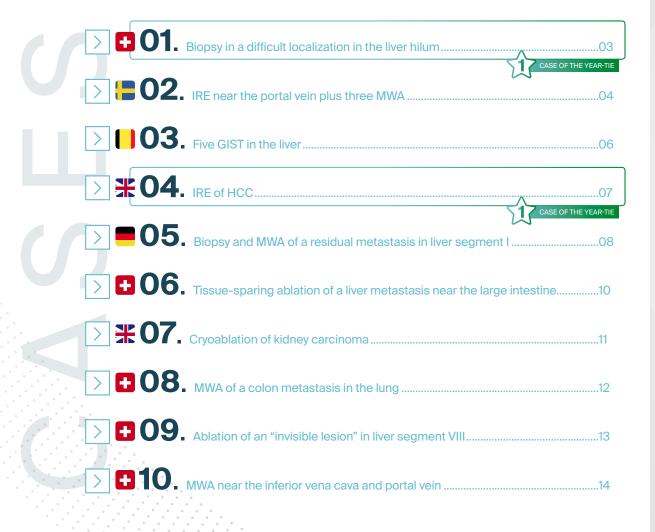




CASCINATION

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Quality Ablation with CAS-One® IR

Reproducible and Standardised Tumour Treatments

More Patients
Better Results*





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CASE 01.

Biopsy in a difficult localization in the liver hilum

CASE OF THE YEAR - TIE

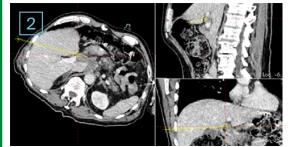
Biopsy in the liver hilum to a suspected lesion with a difficult and long pathway without passing through the portal vein or puncturing the gallbladder. Biopsy was performed with 16G co-axial system with a 18G biopsy needle. Three cylinders were taken from the suspected tissue. The pathology shows a carcinoma with little differential, expressing CDX2 which means it is probably of pancreatic-biliary origin.



Planning scans of the biopsy showing the only possible pathway to the suspected lesion without passing through the portal vein or puncturing the gallbladder

ected lesion ut passing gh the portal Initial condition:

• The patient came to the emergency because he fell frontally on the head probably due to a vasovagal collapse from abdominal pain



CRP and murphy sign were negative

hypodense centre located in the liver hilum

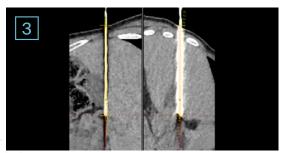
Name: Dr. Lucien Widmer & Dr. Carlo Tappero

Institution: HFR Fribourg, Switzerland

Patient age and sex: 75 years, male

 Two days later in the tumour board the conclusion was to take a biopsy to get a result from the mass. Differential diagnosis was lymphoma/carcinoma

Therefore, a CT was performed which showed a non-homogeneous mass (51x22mm) with a



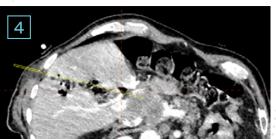
Validation of the position of the biopsy needle

Treatment:

- A previous attempt with ultrasound guidance failed and therefore a biopsy under general anaesthesia with high frequency jet ventilation and the support of CAS-One was considered
- Planning showed only one possible pathway to the suspected lesion, without either passing through the portal vein or puncturing the gallbladder
- Because of the precision required CAS-One IR was used for navigation
- Biopsy was performed with 16G co-axial system with a 18G biopsy needle

Result:

- Three cylinders were taken from suspected mass
- A small bleeding appeared on the post-biopsy scan, however, the following late phase (and angiogram after) showed tamponade
- It was hypothesed that during the biopsy, even though there was a safe distance from the hepatic arteria, a small branch of it was hit
- The pathology shows a carcinoma with little differential, expressing CDX2 which means it is probably pancreatic-biliary origin



Verification after the biopsy was taken

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Cryoablation of kidney carcinom

08 MWA of a colon metastasis in the lung

09Ablation of an "invisible lesion" in liver segmen VIII

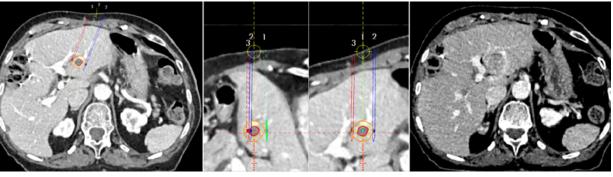
10 MWA near the inferior vena cava and portal vein



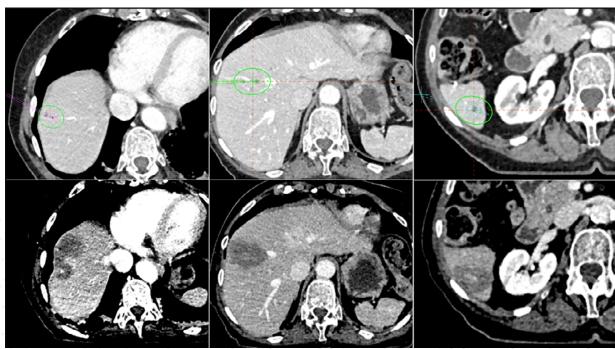
CASE 02.

IRE near the portal vein plus three MWA (1/2)

IRE treatment of a tumour in segment III, located near central bile ducts followed by microwave ablations of two lesions and a suspected third metastasis in proximity to the right liver vein in segment VIII. The post ablation scan shows complete ablation on all four lesions. The complete procedure took 98 minutes (153 minutes counting total anaesthesia time) and the patient stayed over night in hospital, before returning home without any early complications.



Left and center: Planning scan of IRE treatment of tumour in segment III close to bile duct. Right: Ablation validation three months after the intervention.



Top: Planning view of 3 Microwave Ablations
Below: Ablation Validation of 3 Microwave Ablations 3 months after treatment

02IRE near the portal vein plus three MWA

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Biopsy and MWA of residual metastasis in liver segment I

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Tissue-sparing ablation of a liver metastasis near the large intestine

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08 MWA of a colon metastasis in the lun

Ablation of an "invisible lesion" in liver segment VIII

MWA near the inferior vena cava and portal vein



CASE 02.

IRE near the portal vein plus three MWA (2/2)

Name: Dr. Marie Beermann, Dr. Johan Lindeberg & Prof. Dr. Jacob Freedman

Institution: Danderyd Hospital, Stockholm (Sweden)

Patient age and sex: 84 years, female

Initial condition:

- 84 year old woman, who was diagnosted with rectal adenocarcinom in 2019
- Very successful radio/chemotherapy with complete response and thereafter included in a clinical study with watchful waiting
- Six months later she was diagnosed with a gallbladder cancer and had a successful extended resection including segment IVb and V
- After six months a followup CT scan showed three small liver metastasis of up to 10mm in size located in segment III, segment VI and segment VII

Treatment:

- The tumour in segment III was located near central bile ducts. It was biopsied whereafter a 3-electrode IRE was performed with CAS One IR targeting
- Followed by microwave ablation of the other two lesions and a suspected third metastasis in proximity to the right liver vein in segment VIII
- All ablations performed with CAS One IR for targeting
- High-frequency jet ventilation for organ motion control
- An immediate post-operative CT scan with contrast showed complete ablation at all sites
- The purpose of the treatment was curative with this treatment
- The central location of the largest metastasis was a contraindication for thermal ablation
- The other three lesions were treated with microwave ablation, the most effective modality in terms of speed and oncological outcome
- The patient had already undergone two major surgeries within one year without adverse events and could probably have tolerated another one if necessary. But in this case surgical resection was not an option because of the location and number of metastisis.

- There was good evidence that ablative treatment would produce a good oncological outcome compared to resecting the small metastasis, but at a considerably lower cost for the patient in terms of risks and length of stay and rehabilitation
- A biopsy was performed to ascertain the biology of the metastasis as the patient has
 had two resent primaries, colon and gallbladder. Also future treatment options rely
 heavily on the type of metastasis. Radiologically and clinically it was deemed most
 likely to be of colonic origin, which was the reason that all the visible metastasis were
 treated

Result:

• The post ablation scan shows complete ablation on all four lesions. The complete procedure took 98 minutes (153 minutes counting total anaesthesia time) and the patient stayed over night in hospital, before returning home without any early complications. An elevated systolic blood pressure was noted in the postoperativ period, which we have found to be common and transient but without any good explanation and difficult to reverse.

03 Five GIST in the liver



in liver segment I

06

near the large intestine

07

08

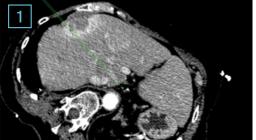
09

10 MWA near the inferior

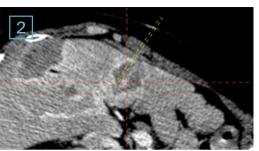


CASE 03 Five GIST in the liver

Tissue sparing approach for five metastatic liver lesions of a Gastrointestinal Stromal Tumor (GIST). All successfully treated in one continueous session. Quality Ablation was preferred over surgical resection to facilitate a speedy recovery after the intervention, offer the patient a better quality of life and preserve options for future treatment, since the patient is likely to develop more metastatic lesions over time.



Ablation Validation after treatment of lesion in Seg I



Ablation Validation of lesion close to gallblader



Ablation Validation of lesion in liver dome



Ablation Validation of lesion in Seg V

Name: Prof. Dr. Thiery Chapelle & Dr. Bart Op de Beeck

Institution: Antwerp University Hospital, Belgium

Patient age and sex: 76 years, female

Initial condition:

- 2014, small intestine perforation with characteristics that fit a Gastrointestinal Stromal Tumor (GIST)
- Diagnosis Gastrointestinal Stromal Tumor (GIST), T2Nx was confirmed through biopsy
- After surgery start adjuvant glivec for three years
- Small intestine was resected after discovery of GIST
- Patient has arterial hypertension
- 2020, five metastatic liver lesions from the GIST

Treatment:

- Treatment strategy: Quality Ablation or major surgical resection
- Decision for minimally invasive intervention to preserve parenchyma for future treatment options, because patient is likely to develop more metastatic lesions over time
- Resection in this case would mean removing several sections of the liver, which would affect the function of the liver and also result in a long hospitalization and recovery.

Result:

 With Quality Ablation the most tissue sparing approach was chosen, to facilitate a speedy recovery, offer the patient a better quality of life and preserve options for future treatment, since the patient is likely to develop more metastatic lesions over time

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IRE near the portal veir

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04IRE of HCC



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Biopsy and MWA of residual metastasis in liver segment I

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Tissue-sparing ablation of a liver metastasis near the large intestine

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Ablation of an "invisible lesion" in liver segment

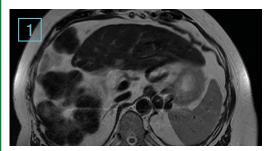
10 MWA near the inferior vena cava and portal vein



CASE 04

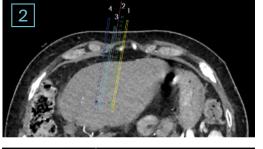
IRE of HCC

This patient presented with an 18mm Hepatocellular Carcinoma (HCC) on the posterior aspect of Segment III of the liver. The ablation technique used was Irreversible Electroporation (IRE) as the tumour was in close proximity to the stomach. Irreversible Electroporation (IRE) is an effective tissue sparing technique which targets the lesion whilst minimising damage to neighbouring structures such as the Stomach, in this particular case. Precise needle positioning is crucial for the IRE treatment to be effective and this was achieved by implementing the CT guidance and navigation capabilities of the CAS-One IR workflow.

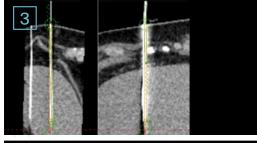


Pre-ablation MR scan of the HCC in Segment III

Transverse planning CT reconstruction



Needle validation scan showing inserted needles



Three months post ablation scan showing the ablation zone (necrosis) in segment III of the liver



Institution: St. James's Hospital, Leeds, United Kingdom

Patient age and sex: 64 years, male

Initial condition:

- History of Hemochromatosis
- Type II diabetes
- Cirrhosis (secondary to Hemochromatosis)

Treatment:

- The IRE treatment was performed under General Anaesthesia with Apnoea
- 4 needles were planned, 3 well positioned, 1 repositioned
- 2 overlapping treatments (1cm pull back on superior needles)
- 90 pulses across each pair of electrode
- 6 pairs treated in total

Result:

- For IRE cases in particular, accurate antenna placement is crucial in order for the treatment to be
 effective. All trajectories have to be aligned parallel to allow the current pulses to induce tumour
 cell death
- Accurate needle placement is difficult when performing the procedure freehand
- CAS-One IR was used as a navigation system in order to achieve great needle-to-target precision
- The three month post ablation control scan shows a complete destruction of the HCC.
- Stomach tissue was spared and left undamaged



02

IRE near the portal vein

03Five GIST in the live

04 IRE of HCC



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Biopsy and MWA of a residual metastasis in liver segment I

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Tissue-sparing ablation of a liver metastasis near the large intestine

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Cryoablation of kidney carcinom

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Ablation of an "invisible lesion" in liver segment VIII

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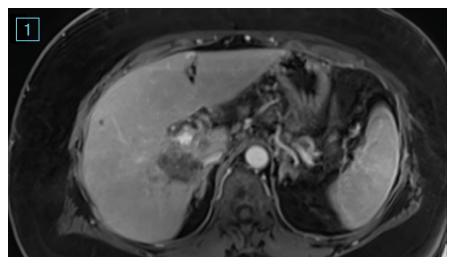
MWA near the inferior vena cava and portal vein



CASE 05.

Biopsy and MWA of a residual metastasis in liver segment I (1/2)

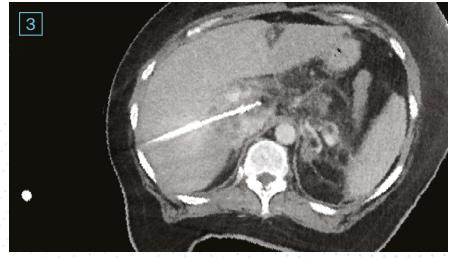
Complex treatment to help a patient with several liver metastasis. In this case a biopsy followed by a microwave ablation of a residual metastasis in segment 1 was performed. Both required extreme precision to not harm critical structures like the inferior caval vein, the right branch of the portal vein and the main bile duct. Successfull treatment was shown on control scans right after the ablation and confirmed by a MRI 6 weeks after the intervention.



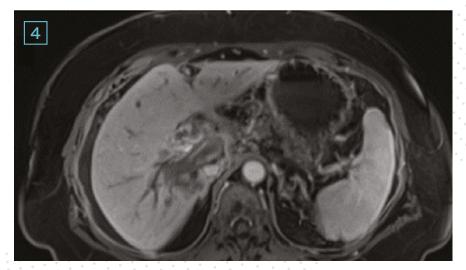
Initial MRI scan showing suspected vital tumour in segment I



Planing of the trajectory for biopsy and ablation also showing the tumour (red), the safety margin (yellow) and the expected ablation zone (green)



Needle validation scan with antenna placed in the tumour



MRI scan confirming complete ablation 6 weeks after treatment

IRE near the portal veir

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05

Biopsy and MWA of a residual metastasis in liver segment I

06

Tissue-sparing ablation of a liver metastasis near the large intestine

07Cryoablation

08 MWA of a colon metastasis in the lun

Ablation of an "invisible lesion" in liver segment

MWA near the inferior vena cava and portal



CASE 05.

Biopsy and MWA of a residual metastasis in liver segment I (2/2)

Name: Dr. Lukas Lürken

Institution: University Hospital Regensburg, Germany

Patient age and sex: 56 years, female

Initial condition:

- Aug 2008 first diagnosis: Breastcancer left, treated with selective resection, radiotherapy and hormone therapy
- Nov 2017 diffuse spinal metastasis diagnosed, treated with radiotherapy. Systemic therapy with several changes due to adverse effects
- Oct 2019 Resection of local recurrent tumor left mamma
- Jan 2020 Liver metastasis in segment VI/I
- Apr 2020 Electrochemotherapy (ECT) of the liver metastasis
- June 2020 residual, progressive tumour tissue in Liver segment 1 in MRI 6 weeks after ECT

Treatment:

- Biopsy of the ablation defect in segment VI as well as biopsy of the suspected vital tumour in segment I, followed by microwave-ablation of the tumour
- Stereotactic navigation with Cas-One IR due to the complicated local tumour situation in Segment I with long trajectory and several "no-go" structures close to the target lesion, such as the inferior caval vein, the right branch of the portal vein and the main bile duct
- First, a 13 G 10 cm coaxial needle was introduced into the liver tissue next to the ECT-Necrosis in segment 6. After biopsy of the necrotic defect with a 14 G SABD biopsy device, the coaxial needle was advanced in the same direction until next to the tumour lesion in segment I, where another biopsy was performed. The biopsy device was removed and a 20 cm microwave antenna was inserted through the coaxial needle. The coaxial needle was retracted for about 5 cm and microwave ablation was performed for 5 minutes with 65 Watts. Control scans directly after the ablation showed complete ablation of the residual tumour. Malignancy of the suspected residual tumour in segment I was confirmed by pathology. The biopsy of the necrotic area in Segment VI showed no vital tumor tissue

Result:

- Complete ablation was achieved, a follow up MRI after 6 weeks confirmed complete ablation
- Unfortunately, the patient's outlook is not good, since she has a multisystemic
 metastatic disease, which showed recurrency under several systemic therapeutic
 regimes. Follow up MRI after 6 weeks showed several new liver metastases and
 a probably new supraphrenic lymph node metastasis. The patient also developed
 cholestasis due to the new liver tumors, requiring percutaneous transhepatic
 cholangiodrainage therapy
- A new regime of combined systemic therapy was discussed

03



05 in liver segment I

06 Tissue-sparing ablation of a liver metastasis near the large intestine

07

08

09

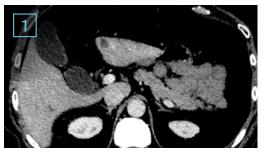
10 MWA near the inferior



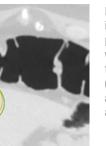
CASE 06

Tissue-sparing ablation of a liver metastasis near the large intestine

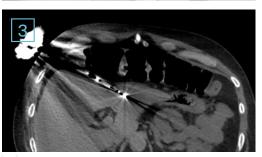
CT-guided microwave ablation of two liver metastasis in the left hepatic lobe in segments III and IVa. Due to the patient history, a tissuesparing procedure was indicated to keep options for further treatment open. At the same time, the ablation in segment III (shown in this case report) in close proximity to the colon requires high precision of the procedure in order to achieve a complete ablation of the malignant tissue without harming the colon.



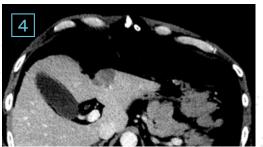
Pre intervention CT scan showing the lesion in segment III of the liver



Lung window image in CT showing the planned intervention with the tumor (red), the safety margin (yellow), the ablation area (green) and adjacent colon



Axial view with trajectory and lesion in segment IVa



Clear markings of the necrotic area at the liver margin

Name: Prof. Dr. Christoph L. Zollikofer

Institution: Kantonsspital Baden, Switzerland

Patient age and sex: 56 years, male

Initial condition:

- 12 2018 Initial diagnosis: primary hepatic and lymphogenic metastatic adenocarcinoma of the sigmoid, TNM stage: pT3, pN2a (4/40), G2, L1, V0, pN1, M1
- 01 2019 Laparoscopic hemicolectomy left and appendectomy
- Second colon carcinoma in the area of the descendosigmoidal transition, pT1, pN2a (4/40), G2, LO, VO, PN
- 02 2019 Conversion chemotherapy ongoing (04 2019)

Treatment:

• The patient is assigned to a bilateral interventional and surgical procedure. First, microwave ablation of the liver metastasis in the left hepatic lobe in segments III (shown in this report) and Va. followed by a right-sided portal vein embolization preoperatively to enlarge the left hepatic lobe

Result:

- Metabolically inactive ablated metastasis in segment III
- Suspected recurrence of metastasis adjacent to the ablated metastasis in segment IVa
- No evidence of extrahepatic metastasis

03



05

06

07 Cryoablation of kidney carcinoma

08

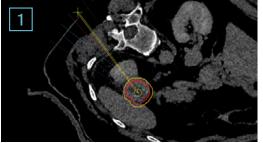
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10 MWA near the inferior



CASE 07 Cryoablation of kidney carcinoma

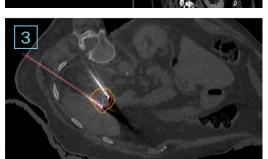
Complex percutaneous intervention with six needles and long trajectories. Cryoablation of a renal cell carcinoma close to pancreatic tail and spleen. CT-guidance and CAS-One IR allowed a very precise placement of all six needles and in result a complete ablation of the entire tumour.



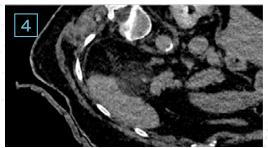
Planning view of the intervention (Axial)



Planning view of the intervention (MPR view)



Needle Placement Control showing high accuracy of probe placement



Confirmation of the cryoablation (Axial)

Name: Prof. Dr. Tze Wah & Dr. Jon Smith

Institution: St. James's Hospital, Leeds, United Kingdom

Patient age and sex: 67 years, male

Initial condition:

- The patient is an ex-smoker with a history of IHD, obesity, COPD, claudication
- Had a femoral stent inserted 17 years ago
- This is a co-morbid patient, not fit for surgery
- Patient presents with a 4.2cm Renal Cell Carcinoma, close to pancreatic tail and spleen
- Upon arrival, an ASA Physical Status Classification of 3 was recorded

Treatment:

• 6 ICE force probe needles (18cm trajectories) were planned using CAS-One IR. Additionally, a tumour biopsy was performed. Once inserted, needle validation showed that needles 1-4 had a lateral error of 2mm and needle 5-6 had a lateral error of 6mm. The 6mm lateral error was due to the difficulty in inserting needles because of needle crowding

Result:

• This was considered a complex case as the tumour was in close proximation to spleen and pancreas. However, overall needle planning and insertion was facilitated using CAS-One IR

03



05 in liver segment I

2

06

near the large intestine

07

08 MWA of a colon metastasis in the lung

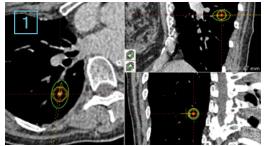
09

10 MWA near the inferior

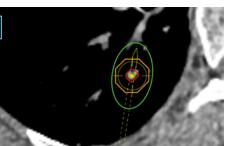


CASE 08 MWA of a colon metastasis in the lung

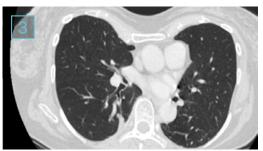
Navigated microwave ablation of a metastasis of the colon that has settled in the lower left lobe of the lung. Planning of the procedure, ablation and verification with CAS-One IR. The CT control scan taken three months after surgery shows no signs of local tumor activity.



Planning scan of the intervention (MPR) showing the tumor (red), safety margin (yellow) and the desired ablation area (green)



Planning axial view with the tumor clearly visible



Control scan three months after surgery: No sign of tumor activity (axial view)



Control scan three months after surgery: No sign of tumor activity (sagittal view)

Name: PD Dr. Anja Lachenmayer & Prof. Dr. Dr. Martin Maurer

Institution: Inselspital, Bern, Switzerland

Patient age and sex: 72 years, female

Initial condition:

- Metastatic carcinoma of the sigmoid colon cT4 cN0 cM1, diagnosed 06/2017
- Histology: moderately differentiated adenocarcinoma of the sigmoid (G2), diameter 5.5cm. tumor-free oral aboral and circumferential resection margin
- Emergency laparoscopically assisted oncological sigmoid resection, descendo rectostomy, hysterectomy, bilateral salpingectomy following tumor rupture in uterus
- Atypical partial liver resection segment II/III (2x), segment IVa, segment V, segment IVb, segment I following bilateral liver metastases
- CT thorax/abdomen/pelvis (02/2019): Slight increase in size of the known intrapulmonary round foci in the left upper lobe dorsobasal and lower lobe dorsobasal. Subcapsular hematoma in liver segment VI, constant in size compared to the previous examination. No evidence of newly occurring liver metastases
- Uniportal, anatomical segment VI resection and radical mediastinal lymphadenectomy left with pulmonary metastasis in the apical lower lobe on the left

Treatment:

Navigated microwave ablation of a colon metastasis in the lower left lobe of the lung

Result:

• The control CT three months after treatment shows no tumor activity

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Biopsy and M\

Biopsy and MWA of residual metastasis in liver segment I

06

Tissue-sparing ablation of a liver metastasis near the large intestine

O7
Cryoablation
of kidney carcinoma

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09Ablation of an "invisible lesion" in liver segment VIII

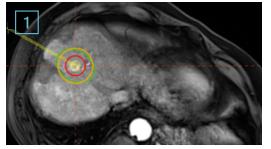
10 MWA near the inferior vena cava and portal vein



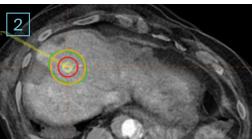
CASE 09.

Ablation of an "invisible lesion" in liver segment VIII

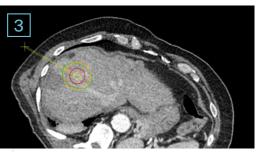
CT-guided and navigated biopsy followed by microwave ablation of a hepatocellular carcinoma. Treatment thanks to image fusion of MRI and CT imaging on CAS-One IR. Control MRI shows complete necrosis of HCC in segment VIII.



MRI scan showing the lesion in the center of the three circles: red (tumour), yellow (safety margin), green (ablation volume)



50/50 MRI and CT scan



CT scan not showing the lesion



Control scan after the ablation showing the necrosis at the treatment area Name: PD Dr. Anja Lachenmayer & Dr. Nando Mertineit

Institution: Inselspital, Bern, Switzerland

Patient age and sex: 63 years, male

Initial condition:

- Initial diagnosis: Multifocal hepatocellular carcinoma (HCC), stage BCLC B
- Admission of the patient to hepatology. Diagnosis: cirrhotic liver and multifocal HCC. Start of systemic therapy with sorafenib and recommendation for accompanying microwave ablation for local tumor control
- Aim of «downstaging» in order to qualify the patient for liver transplantation according to the Milan criteria
- Microwave ablation in segments IVb and VI (In the course of treatment CAS-One IR was used for all ablations)
- Additional HCC suspect lesions in segments II, III and VII

Treatment:

 CT-guided and navigated biopsy followed by microwave ablation of an «invisible» lesion in liver segment VIII. Fusion of MRI and CT imaging to treat the lesion

Result:

The «invisible» lesion was completely ablated (Figure 4). Subsequently, the patient is examined
for HCC suspicious lesions at regular appointments to check whether the criteria for his
classification have changed or whether new ablations/treatments are necessary.

CASE 10.

MWA near the inferior vena cava and portal vein (1/2)

02

03



Biopsy and MWA of a residual metastasis

06

07

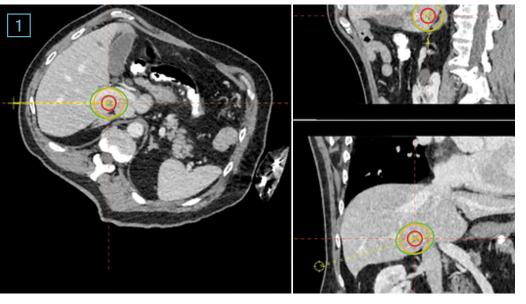
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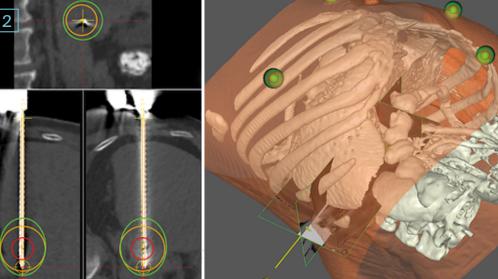
10 MWA near the inferior vena cava and portal vein



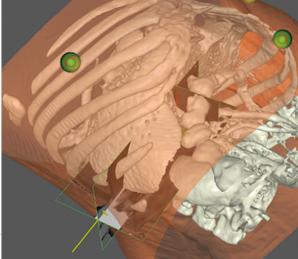
Navigated ablation of a difficultly located lesion in segment VI of the liver under the glisson capsule between the portal vein and the vena cava. Ablation was the only possible treatment because the patient refused chemotherapy. No vessels damaged during intervention. Complete ablation of the lesion on the control CT.



Planning scan of the intervention (MPR)



Validation of needle trajectory and needle position



02

IRE near the portal veir plus three MWA

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04IRE of HCC



Biopsy and MWA of residual metastasis in liver segment I

06

Tissue-sparing ablation of a liver metastasis near the large intestine

07Cryoablation of kidney carcinoma

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09Ablation of an "invisible lesion" in liver segment VIII

MWA near the inferior vena cava and portal

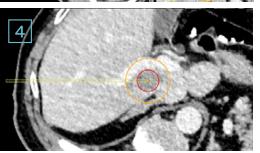


CASE 10.

MWA near the inferior vena cava and portal vein (2/2)



CT scan after ablation with complete tumor treatment in axial, sagittal and coronal view



CT scan directly after ablation with ablation zone (hypodense) and planned safety margin (yellow) Name: Dr. Carlo Tappero

Institution: HFR Fribourg, Switzerland Patient age and sex: 58 years, male

Initial condition:

Moderately differentiated adenocarcinoma of the lower rectum, classified as cT3 uN1 cM0, mutated KRAS gene, diagnosed quarter 2, 2018

- MRI of the pelvis, quarter 2, 2018: Tumour of the lower rectum, located about 5.5 cm from the anal edge and 2 cm from the upper part of the anal sphincter. The tumour infiltrates the right perirectal fat, which is classified as T3 N+ in the lower pole and is located 2 cm above the upper part of the anal sphincter
- Post-Radiochemotherapy status with Xeloda, quarter 2, 2018
- Ultra-low anterior post-resection status by laparotomy with manual colo-anal anastomosis and protective ileostomy, quarter 3, 2018, complicated by the conservatively treated anastomosis load.
 Postoperative stage ypT3 ypN1c (tumour deposition) (0/25) R0 V0 pN0 R0. Tumour regression degree TR3
- Status after 9 cycles of palliative chemotherapy with FOLFOX (refusal of treatment with Avastin), quarter 4, 2018 to quarter 1 2019 followed by 6 cycles of chemotherapy with 5-FU / Leucovorin until quarter 2, 2019

Treatment:

- Decision for a navigated procedure with CAS-One because the lesion is located in segment VI of
 the liver, under the glisson capsule and between the portal vein and the vena cava. Although the
 lesion was clearly identifiable under ultrasound, no access could be planned without damaging
 other vessels. With CAS-One, optimal access to the lesion could be planned and the procedure
 performed according to plan.
- Ablation was the only possible treatment as the patient refused chemotherapy.

Result:

• The control CT shows the complete ablation of the lesion

Benefits of Quality Ablation with CAS-One® IR



Enhanced Reliability and Accuracy with CT/MRI Planning & Navigation¹⁻³



Treat More Patients with Challenging Tumour Cases²⁻⁴



Consistently low complication and significantly reduced recurrence rates³⁻⁵





^{2.} Beyer LP et al.: Stereotactically-navigated IRE compared to conventional IRE, PeerJ 2016

^{5.} Beermann, M., et al.: 1000 consecutive ablation sessions in the era of computer assisted image guidance, Euro J Rad O 2018



^{3.} Tinguely P et al.: Stereotactic Image-Guided Microwave Ablation for Malignant Liver Tumors, Front. Oncol 2020

^{4.} Lachenmayer et al.: Stereotactic image-guided microwave ablation of hepatocellular carcinoma, Liver Int. 2019

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