Radioablation of Upper Abdominal Malignancies by CT-Guided, Interstitial HDR Brachytherapy: A Multivariate Analysis of Catheter Placement Assisted by Ultrasound Imaging

Radioablation abdomineller Malignome durch CT-geführte, interstitielle HDR-Brachytherapie: Multivariate Analyse der ultraschallassistierten Katheterimplantation

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ZUSAMMENFASSUNG

Ziel Evaluierung der Ultraschallbildgebung (US) zur Katheterplatzierung bei der interstitiellen Brachytherapie (iBT) abdomineller Malignome als Alternative zur computertomografischen (CT) Fluoroskopie.

Material und Methoden Die Katheteranlage zur iBT erfolgte nach Möglichkeit mittels Sonografie bei 52 konsekutiven Patienten mit 82 abdominellen Tumoren (Leber n = 62, Niere n = 16, Peritoneum n = 4) unterschiedlicher Entitäten. Es wurden Läsionssichtbarkeit, Lokalisation, Tiefe und Größe sowie Dosimetrie erfasst. Der Vergleich zwischen CT- und ultraschallassistierter Katheteranlage erfolgte mittels Fisher's exaktem Test für Häufigkeiten und U-Test für Sichtbarkeit und Dosimetrie. Faktoren für die Anwendung der Sonografie wurden in einer multivariaten Regression bestimmt. $p < 0{,}05$ wurde als signifikant betrachtet.

Ergebnisse 150 Katheter (1–6 pro Läsion, mittlerer Diameter 3,6 ± 2,4 cm) wurden eingebracht, CT-Fluoroskopie wurde bei 44 Kathetern und Ultraschall bei 106 Kathetern angewendet. Die Sichtbarkeit war anhand einer 5-Punkte-Likert-Skala signifikant besser (median 2 vs. 3; $p = 0{,}011$) und die effektive Dosis wurde signifikant reduziert, wenn Ultraschallführung anwendbar war (median 1,75 vs. 8,9mSv; $p = 0{,}014$). In der multivariaten Regressionsanalyse konnten ein größerer Läsionsdiameter sowie eine kaudale Lokalisation im Zielorgan als Faktoren zur Vorhersage der Ultraschallanwendung bei der iBT identifiziert werden.

Fazit Die Sonografie ist eine nützliche Bildgebungsmodalität bei der Katheteranlage zur CT-gesteuerten Brachytherapie abdomineller Malignome. Bei größeren Läsionen in den kaudalen Lebersegmenten oder der unteren Nierenhälfte können eine bessere Läsionssichtbarkeit und reduzierte Dosis erwartet werden.

Kernaussagen:

- Die ultraschallgestützte Katheterplatzierung bei der CT-geführten Brachytherapie abdomineller Malignome erhöht signifikant die Läsionssichtbarkeit.
- Prädiktoren einer erfolgreichen Ultraschallanwendung sind größere Läsionen in den unteren Segmenten der Leber und Nieren.
- Durch die Reduzierung der CT-Fluoroskopie kann die Strahlenexposition des medizinischen Personals indirekt gesenkt werden.

ABSTRACT

Purpose To evaluate the use of ultrasound (US) during catheter placement in interstitial brachytherapy (iBT) of abdominal malignancies as an alternative to computed tomography (CT) fluoroscopy.

Materials and Methods Catheter placement for CT-guided iBT was, if US visibility was sufficient, assisted by sonography in 52 consecutive patients with 82 lesions (liver N = 62; kidney N = 16; peritoneum N = 4) of various malignancies. We collected data on lesion visibility, location, depth, size, and dosimetry. Comparison of CT fluoroscopy versus US-assisted catheter placement was performed by Fisher's exact test for frequencies and U-test for lesion visibility and dosimetric data. Factors predicting the utility of sonography were determined in a lesion-based multivariate regression analysis. A p-value < 0.05 was regarded as statistically significant.

Results 150 catheters (1 to 6 per lesion; mean diameter 3.6 ± 2.4 cm) were implanted. CT fluoroscopy was used for 44 catheters, and US was used for 106 catheters. Lesion visibility assessed by 5-point Likert scale was significantly better in US (median 2 vs. 3; p = 0.011) and effective dose was significantly reduced if US guidance was applicable (median 1.75 vs. 8.19 mSv; p = 0.014). In a multivariate regression analysis, we identified increased lesion size and caudal location within the target organ to independently predict the utility of ultrasound in catheter placement for iBT.

Conclusion Sonography is a helpful technique to assist CT-guided interstitial brachytherapy of upper abdominal malignancies. Especially for larger lesions localized in the lower liver segments or lower half of the kidney, superior visibility can be expected. As the effective dose of the patient is also reduced, radiation exposure of the medical staff may be indirectly lowered.

Key Points:
- Ultrasound-assisted catheter placement in CT-guided brachytherapy of upper abdominal malignancies significantly improves lesion visibility.
- Predictors of successful ultrasound application are larger lesions within the lower portion of the liver and kidney.
- By reducing the need for CT fluoroscopy during intervention, radiation exposure to the medical staff may be indirectly lowered.

Citation Format
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Introduction

Local ablative treatments are increasingly included in the treatment of common abdominal malignancies, e. g., colorectal cancer liver metastases, renal cell cancer, and hepatocellular carcinoma [1–3]. In most institutions, thermal ablation techniques, such as radiofrequency ablation (RFA) or microwave ablation (MWA), are applied under image guidance by ultrasound (US) and CT fluoroscopy (CTF) in the treatment of lesions with a diameter of up to 3 or 4 cm [4]. Beside the size of targeted tumors, thermal ablation techniques are limited by cooling effects of adjacent vessels and the proximity of heat-vulnerable structures (e. g., bile duct, renal pelvis) [5–7].

Interstitial high-dose rate (HDR) brachytherapy poses an alternative ablation technique by delivering ablative doses of radiation ("radioablation") through percutaneously applied irradiation catheters in a single fraction [8]. Advantages over thermal ablation include a higher conformality of the ablation zone and no interference by surrounding vessels or heat-sensitive organs [9].

Still, precise catheter placement in interstitial brachytherapy (iBT) is just as crucial as applicator positioning in RFA or MWA to achieve successful ablation and depends on good lesion visibility during the intervention [10]. While most interventions today are performed under CT fluoroscopy and iBT furthermore requires a CT-based 3 D irradiation plan, the application of ultrasound imaging might bring additional value as initial studies suggest [11]. When choosing the imaging modality for a desired intervention by axial tomography studies, the utility of sonography is difficult to predict, and hybrid interventional suites are still unavailable in most institutions.

In this study, we want to elucidate factors predicting the effectiveness of ultrasound in interstitial brachytherapy that would justify the addition of a sonography unit or could allow an intervention under ultrasound guidance alone.

Materials and Methods

Patient cohort

The study was conducted in accordance with the Declaration of Helsinki and was authorized by the institutional review board. A total of 52 patients were prospectively recruited after given written informed consent for participation in the study. 32 males and 20 females with a median age of 72.5 years (range: 47–89 years) had 82 lesions (liver N = 62, kidney N = 17, peritoneum N = 4) to undergo CT-guided interstitial brachytherapy. Tumor entities included colorectal cancer (N = 19), renal cell cancer (N = 15), hepatocellular carcinoma (N = 14), cholangiocelluar carcinoma (N = 11), breast cancer (N = 4), and pancreatic cancer (N = 3). 14 cases underwent surgical resection at the targeted organ prior to iBT. Concomitant liver pathologies were cirrhosis (N = 19) and steatosis (N = 5) as assessed by hepatobiliary MRI.

The inclusion criteria were:

I. scheduled CT-guided iBT for the local ablation of one or more cancer lesions,
II. ineligibility to undergo surgical resection,
III. Eastern Cooperative Oncology Group (ECOG) performance status 0 to 2,
IV. life expectancy > 6 months
V. sufficient laboratory parameters to undergo interventional procedures (international normalized ratio < 1.5, partial thromboplastin time < 50 s, hemoglobin > 6.0 mmol/l, thrombocyte count > 50 Gpt/l).

A summary of patient characteristics is given in ▶ **Table 1**.

► **Table 1** Patient and lesion characteristics of the study cohort. Comparison of cases with ultrasound-assisted vs. CT fluoroscopy (CTF) only interventions, U-test for continuous/categorical variables, and Fisher's exact test for nominal variables.

► **Tab. 1** Patienten- und Läsionscharakteristika der Studienkohorte. Vergleich der Fälle mit ultraschallassistierter vs. allein CT-fluoroskopisch durchgeführter Intervention. U-Test für stetige und kategoriale Variablen, exakter Test nach Fisher für nominale Variablen.

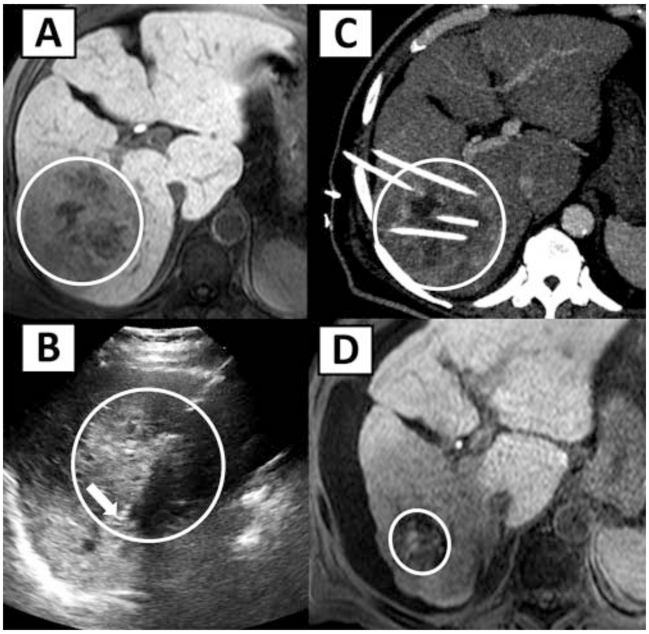
patient variables (N = 52)	**N (%) or median (range)**	**p-value***
age	72.5y (47–89y)	0.10
sex (m/w)	N = 32 (62 %) / N = 20 (38 %)	0.23
number of lesions	N = 83	0.43
major complications	N = 1 (2 %)	1.0
minor complications	N = 1 (2 %)	1.0
ECOG	1 (0–2)	0.75
follow-up (months)	9 m (0–33 m)	
lesion variables (N = 82)	**N (%) or median (range)**	**p-value***
tumor entities		0.15
▪ colorectal cancer	N = 26 (32 %)	
▪ renal cell cancer	N = 16 (20 %)	
▪ hepatocellular carcinoma	N = 19 (23 %)	
▪ cholangiocarcinoma	N = 14 (17 %)	
▪ breast cancer	N = 4 (5 %)	
▪ pancreatic cancer	N = 3 (4 %)	
target organs		0.08
▪ peritoneum	N = 4 (5 %)	
▪ kidney	N = 17 (20 %)	
▪ liver – w/cirrhosis – w/steatosis	N = 62 (75 %) N = 19 (31 %) N = 5 (8 %)	
prior operations of target organ	N = 14 (17 %)	0.09
total number of catheters	N = 150	0.53
▪ CTF only	N = 44	
▪ US-assisted	N = 106	
diameter	2.9 cm (0.5–14.1 cm)	**< 0.001****
CT fluoroscopy		
▪ CTDIvol	361 mGy (0–4039 mGy)	**0.016****
▪ DLP	215 mGy*cm (0–2412 mGy*cm)	**0.012****
▪ effective dose	3.2 mSv (0–36.2 mSv))	**0.014****
▪ fluoroscopy time	38.7 s (0–421 s)	**0.016****
dose to PTV (D100)	19 Gy (8.3–26.9 Gy)	0.43
target dose achieved	N = 67 (81 %)	0.64
local tumor control	N = 75 (90 %)	1.0

* p-values comparing patients/lesions with US-assisted vs. CTF only catheter placement.
** p < 0.05 considered statistically significant.

Technique of interstitial brachytherapy

All interventional catheter placement was performed under local anesthesia and conscious sedation using fentanyl and midazolam. Antiemetic prophylaxis with 8 mg dexamethasone and 8 mg ondansetron was administered intravenously. Antibiotic prophylaxis was not routinely required.

Lesions were punctured under image guidance (see below) with an 18G coaxial needle and subsequently 6F angiographic catheter sheaths (Terumo Radifocus Introducer II, Terumo



▶ **Fig. 1** Patient case out of the study population: hepatocellular carcinoma (HCC) in liver cirrhosis scheduled for interstitial brachytherapy (tumor mass highlighted by circles). **A** Pre-treatment hepatobiliary MRI demonstrating a large nodule with a diameter of 10 cm; **B** peri-interventional sonography depicting the tip of a brachytherapy catheter inserted under ultrasound guidance; **C** maximum intensity projection (MIP) of irradiation planning CT performed directly after insertion of 5 catheters under US guidance; **D** follow-up hepatobiliary MRI after 6 months demonstrating significant tumor shrinkage.

▶ **Abb. 1** Fallbeispiel aus der Studienkohorte: Hepatozelluläres Karzinom in Leberzirrhose mit geplanter interstitieller Brachytherapie (Tumor jeweils als Kreis markiert). A Präinterventionelles MRT der Leber mit 10 cm großem Knoten; B Periinterventioneller Ultraschall zeigt die Spitze eines Brachytherapiekatheters, der unter sonographischer Sicht eingebracht wurde; C Maximalintensitätsprojektion (MIP) des CT zur Bestrahlungsplanung direkt nach Einbringung von 5 Kathetern unter Ultraschallsicht; D MRT der Leber zur Nachsorge nach 6 Monaten zeigt eine signifikante Tumorschrumpfung.

Europe, Leuven, Belgium) were inserted using Seldinger's technique via a stiff guidewire (Amplatz SuperStiff™, Boston Scientific, Marlborough, USA). Then, 6F irradiation catheters were placed within the sheaths and fixed with a suture. Depending on the shape and location of the target lesions (N = 83), a total of 150 catheters were placed to accommodate a sufficient geometry of the ablation zone while simultaneously avoiding radiation to adjacent organs. After successful catheter insertion, a CT data set (axial slices with thickness of 3 mm) was acquired and transferred to the irradiation planning tool (Oncentra Brachy, Elekta Instrument AB, Stockholm, Sweden). Gross tumor volume (GTV) was contoured manually and the clinical target volume (CTV) was automatically generated by adding a 5-mm safety margin [12]. Due to the fixation of the irradiation catheters in the targeted lesions, respiratory movement was omitted, and CTV was adopted as the planning target volume (PTV). High-dose-rate (HDR) irradiation was performed in a single fraction using an Iridium192 source in the afterloading technique to achieve "radioablation". Ablative doses for the PTV were defined as 25 Gy for colorectal carcinoma, 20 Gy for cholangiocarcinoma, and 15 Gy for all other entities according to contemporary literature [13–15]. Dose constraints for organs at risk (OAR) have been published previously [11]. After the irradiation, removal of catheters and sheaths was performed with the insertion of a gelatin sponge into the catheter path to prevent post-interventional bleeding. A representative case of the study cohort is depicted in ▶ **Fig. 1**.

Image guidance by CT fluoroscopy and ultrasound

To achieve precise placement of the catheter sheaths incorporating the irradiation catheters within a target lesion, initial needle placement as well as necessary monitoring of the guide wire and catheter sheaths need to be performed under image guidance. In the daily routine, visualization was performed by CT fluoroscopy (Aquillion, Canon Medical Systems, Neuss, Germany) with 120 kVp/30 mAs, 0.5 s rotation time, 6-mm single-slice acquisition, and an image matrix of 512 × 512. Image reconstruction was based on an iterative image reconstruction algorithm [16].

Within the study, any possible step during catheter placement was performed utilizing sonography (EPIQ7, Philips Medical Systems, Amsterdam, The Netherlands) with low-frequency ultrasound transducers (1–5 MHz convex, 1–6 MHz matrix). Needle guidance or free-hand approach during ultrasound-assisted puncture was used at the discretion of the interventional radiologist. Final radiotherapy planning was based on a CT scan in all cases (planning algorithm see above).

Data acquisition and statistical analysis

Prospective data collection and analysis were approved by the local ethics committee.

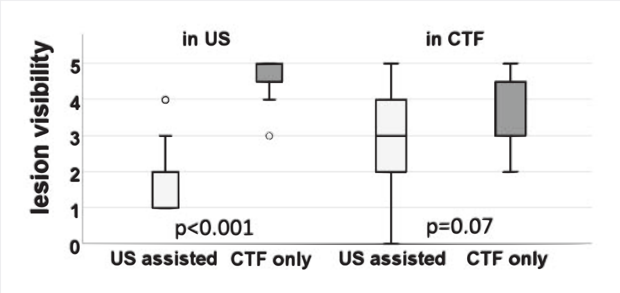
We recorded patient and lesion characteristics, CTF parameters (fluoroscopy time, CDTIvol, DLP) and ablation dosimetry (CTV, D100). Additionally, effective doses (E_{eff}) were calculated based on the dose-length product (DLP) weighted with a body region-specific conversion factor [16]:

$E_{eff} = DLP * 0.015\, mSv/(mGy * cm)$.

Lesion positions were determined on the CT scan acquired for irradiation planning, and the lesion depth within the abdomen and the thickness of the body wall were measured on axial slices. The visibility of the target lesion on CTF and US was stated by the interventional radiologist according to a 5-point Likert scale (1 corresponding to best possible visualization – 5 equaling no vision of the lesion/intervention using anatomical landmarks).

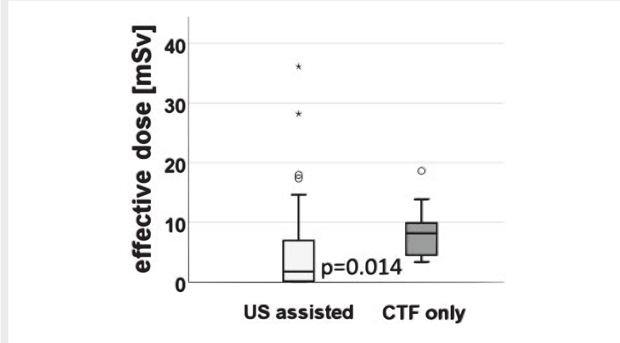
Major and/or minor complications were categorized according to the Society of Interventional Radiology (SIR) classification. All data were transferred to SPSS (IBM SPSS Statistics, IBM Deutschland GmbH, Ehningen, Germany) for descriptive and statistical analysis.

The median and range were used to characterize parametric or categorical variables, comparisons were performed with the Mann-Whitney U-test. Fisher's exact test was applied to compare frequencies of nominal variables. All pre-treatment variables obtainable from a routine CT/MRI scan or patient data to predict the usefulness of ultrasound were tested in a univariate linear



▶ **Fig. 2** Visibility of target lesions in ultrasound (US) and CT fluoroscopy (CTF) as rated by the interventional radiologist. Comparison of lesions with US-assisted catheter placement (US-assisted) versus catheter placement under CT fluoroscopy alone (CTF only) in each imaging modality. P-values from Mann-Whitney U-test.

▶ **Abb. 2** Sichtbarkeit der Zielläsionen im Ultraschall (US) und in der CT-Fluoroskopie (CTF) nach Bewertung durch den Interventionsradiologen. Vergleich der Läsionen mit ultraschallassistierter (US assisted) gegenüber rein CT-fluoroskopischer (CTF only) Katheterplatzierung in der jeweiligen Modalität. P-Werte aus dem Mann-Whitney U-Test.



▶ **Fig. 3** Effective dose as calculated from the dose-length product (DLP). Comparison of lesions with US-assisted catheter placement (US-assisted) versus catheter placement under CT fluoroscopy alone (CTF only) in each imaging modality. P-values from Mann-Whitney U-test.

▶ **Abb. 3** Effektive Dosis berechnet aus dem Dosis-Längen-Produkt (DLP). Vergleich der Läsionen mit ultraschallassistierter (US assisted) gegenüber rein CT-fluoroskopischer (CTF only) Katheterplatzierung in der jeweiligen Modalität. P-Werte aus dem Mann-Whitney U-Test.

regression analysis. All factors with $p < 0.1$ were finally included in a multivariate regression analysis. For all statistical tests, $p < 0.05$ was considered significant and $p < 0.01$ highly significant.

Results

Treatment characteristics and follow-up

52 patients were treated by interstitial HDR brachytherapy in 83 lesions with a median diameter of 2.9 cm (range: 0.5–14.1 cm) and a total of 150 brachytherapy catheters were placed. The median ECOG performance status was 1 at the time of intervention. In 14 lesions, target organs had undergone prior surgical therapies while 7 lesions were local recurrences after surgery. Catheter placement was performed solely under CT fluoroscopy in 44 cases (29.3 %) while US assistance was applicable in 106 catheters (70.7 %), resulting in 50.6 % of lesions undergoing intervention under sonography guidance alone. The lesion diameter was significantly larger in the US-assisted group (median 3.6 vs. 2.3 cm, $p < 0.001$), but no statistically significant difference was found for the number of catheters implanted ($p = 0.138$).

With a median dose to PTV of 19 Gy (range: 8.3–26.9 Gy), the individual target dose to achieve radioablation was achieved in 67 lesions (81 %). During a median follow-up of 9 months (range: 0–33 months), local tumor control was recorded in 75 lesions (90 %) without a significant difference between CTF and US-assisted interventional guidance ($p = 1.0$). A summary of lesion and treatment characteristics is given in ▶ **Table 1**.

One major complication and one minor complication occurred: A patient with interstitial brachytherapy of renal cell carcinoma experienced acute bleeding of the punctured mass and underwent coil embolization upon detection. The patient was hemodynamically stable and underwent 12 hours of monitoring at the intensive care unit for safety reasons. Another patient developed a local hematoma of the renal capsule without any symptoms or requirement of invasive or noninvasive measures.

As dose constraints by organs at risk (OAR) were strictly applied in all cases, no late effects of irradiation were observed. The overall frequency of major and minor complications was 2 % per patient and 1.2 % per lesion.

Lesion visibility and dosimetry

As rated by the interventional radiologist, the visibility of each lesion was recorded in ultrasound and CT fluoroscopy irrespective of the imaging method finally used during puncture and catheter insertion. Overall, visibility was significantly better in ultrasound (median 2, range: 1–5) than in CTF (median 3, range: 1–5) utilizing a 5-point Likert scale with best presentation rated as 1 ($p = 0.011$). Comparing lesions with US-assisted catheter insertion versus CTF guidance only, visibility was superior in sonography (median 2 vs. 3, $p < 0.001$) while it was not in CTF (median 5 vs. 3, $p = 0.07$), see ▶ **Fig. 2**.

Dose exposure by CTF according to CTDIvol (median 188.5 vs. 909.1 mGy, $p = 0.016$) and DLP (116.9 vs. 546.2 mGy*cm, $p = 0.012$) was distinctly lowered as fluoroscopy time was significantly reduced (27.5 vs. 68.6 s, $p = 0.016$). Calculating the cumulative effective doses, best possible application of sonography during catheter insertion yielded a highly significant reduction (median 1.75 vs. 8.19 mSv, $p = 0.014$) as depicted in ▶ **Fig. 3**.

Regression analysis of predictive factors

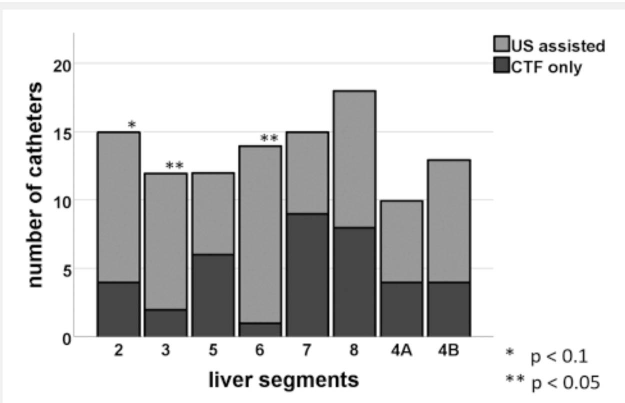
We then sought to determine factors that could predict the applicability of sonography prior to the scheduled brachytherapy without dedicated evaluation of US visibility. The dependent variable was the portion of catheters placed under sonography guidance per lesion. All accessible variables from standard clinical

▶ **Table 2** Linear regression analysis of factors to predict the utility of ultrasound imaging in lesions scheduled for CT-guided HDR brachytherapy: Dependent variable is the proportion of catheters placed under sonography per lesion.

▶ **Tab. 2** Lineare Regressionsanalyse prädiktiver Faktoren für die Anwendbarkeit des Ultraschalls bei Läsionen in der CT-gesteuerten HDR-Brachytherapie. Abhängige Variable ist der Anteil unter Sonographie eingebrachter Katheter pro Läsion.

	univariate analysis		multivariate analysis	
variable	**standardized ß**	**p-value**	**standardized ß**	**p-value**
age	–0.178	0.207		
sex	0.113	0.426		
prior operation of target organ	**–0.190**	**0.088***	–0.104	0.331
access route (transcostal/subcostal)	**0.257**	**0.02***	0.18	0.118
abdominal wall thickness	–0.02	0.859		
abdominal lesion depth	**–0.248**	**0.025***	–0.004	0.976
lesion diameter	**0.196**	**0.078***	**0.228**	**0.043****
lesion located within target organ				
▪ cranial/caudal***	**–0.327**	**0.003***	**–0.299**	**0.009****
▪ central/peripheral	–0.144	0.207		
subgroups of liver lesions in				
▪ liver cirrhosis	0.028	0.831		
▪ liver steatosis	0.112	0.386		

* p < 0.1 to be included in the multivariate analysis.
** p < 0.05 regarded as statistically significant in the multivariate analysis.
*** cranial location defined as liver segments 2/4A/7/8 or upper half of the kidney.



▶ **Fig. 4** Subgroup of liver lesions. Columns depicting the number of catheters placed under sonography guidance (US-assisted) versus CT fluoroscopy guidance (CTF only) in each liver segment.

▶ **Abb. 4** Subgruppe der Leberläsionen. Die Balken entsprechen der Anzahl der Katheter, die unter Ultraschallsicht (US-assisted) bzw. rein unter CT-Fluoroskopie (CTF) pro Lebersegment implandiert wurden.

evaluation (patient demographics and history, routine imaging) were included in a univariate linear regression analysis. Prior operations involving the target organ, access route (transcostal vs. subcostal), abdominal lesion depth, lesion diameter and lesion location (cranial vs. caudal part of the target organ) reached a p-value of at least 0.1 and were subsequently processed in a multivariate regression analysis. Here, only lesion diameter (p = 0.043) and lesion location (p = 0.009) had a significant impact on the number of catheters implantable under sonographic assistance.

An overview of the regression analysis is given in ▶ **Table 2**.

Subgroup of liver lesions

As the majority of patients underwent liver-directed interstitial brachytherapy (75 % of all lesions) and tumor location can be further assessed by the segmental anatomy, we analyzed this subgroup of liver lesions. There was no difference in the frequency of primary (N = 29) vs. secondary liver malignancies (N = 33) in the Fisher's exact test (p = 0.78). Furthermore, the incidence of liver steatosis (N = 4 vs. N = 1) or cirrhosis (N = 13 vs. N = 6) was not significantly different between US-assisted interventions versus CTF only (p = 1.0). The number of catheters inserted per imaging modality was then compared by the Wilcoxon test in each segment. A tendency to increased US application was noted in segment 2 while a statistically significant increase was found for liver segments 3 and 6. The distribution of liver lesions to the liver segment and corresponding techniques of image guidance during catheter placement are illustrated in ▶ **Fig. 4**.

Discussion

The value of different imaging techniques like computed tomography fluoroscopy (CTF), magnetic resonance imaging (MRI), and ultrasound (US) has been described in the context of thermal ablation in several tumor entities [17, 18]. Most of these studies compare these modalities head-to-head but often in a retrospective fashion [19–21].

Besides our initial experience in 12 patients, no investigation on the utility of ultrasound imaging during puncture and catheter placement in CT-guided interstitial brachytherapy of hepatic or renal masses has been published to date [11]. As a CT data set is mandatory for 3 D treatment planning, our approach aims to prospectively append sonography to our routine procedure of CTF guidance for the insertion of irradiation catheters with subsequent CT scan all in the same room. Thus, we emphasized the analysis on the possibility to determine the technical setup (US-assisted vs. CTF only) without dedicated sonographic evaluation of each lesion prior to the intervention.

As about 50 % of the lesions were punctured under US guidance alone and at least part of the intervention could be performed using sonography in another 20 %, we achieved a significant dose reduction compared to lesions completely requiring CTF for catheter placement as US visibility was too low. The multivariate regression analysis demonstrated that larger lesions in the lower half of the targeted organ were significantly more accessible for sonography guidance which is consistent with general experience in US-guided interventions. Contrarily, typical factors known to impair sonographic visibility like the patient's body constitution (body wall thickness and corresponding lesion depth within the body) had no significant impact. Hence, such patients should not be precluded from US-assisted catheter placement in interstitial brachytherapy.

Comparable studies in other local ablative therapies are scarce, yet McGahan et al. determined US only vs. US plus CT as image guidance in RFA of renal masses by pretreatment imaging [22]. Similar to our results, about half of their patients could be treated using sonography alone. In a linear regression analysis, tumor location had no influence on treatment outcome given that a pretreatment evaluation of ultrasound visibility was performed. A retrospective report from Kan et al. covers the special situation of RFA in hepatocellular carcinoma in the hepatic dome after transarterial chemoembolization with lipiodol/doxorubicin [23]. They achieved excellent results of local tumor control in this unfavorable tumor location with a significant reduction of procedural time by a combination of US/CT guidance for probe positioning. Unfortunately, prior imaging also included sonography and it is not stated how patients were exactly allocated to the treatment groups.

As a similar limitation of our prospective single arm trial, no randomization was performed while including consecutive patients scheduled for interstitial brachytherapy in our department. Thus, independent assessment of the guidance techniques during catheter placement could not be guaranteed and both interventional radiologists were prone to a selection bias. As the overall visibility of malignant lesions in US and/or CTF can only be judged genuinely by the performing physician, rating according to a Likert scale has a methodical limitation to only one reviewer without the possibility to analyze interobserver reliability.

Nonetheless, the individual addition of sonography to a CT-guided intervention follows the ALARA principle ("as low as reasonably possible") with the only practical restriction of this approach being economical as a second machine is absorbed during the time of intervention. As the development of hybrid imaging systems continues, the integration of a sonography module into an interventional CT suite might be a valuable solution.

Summary

Our results suggest the addition of ultrasound imaging to CT-guided interstitial brachytherapy of upper abdominal malignancies whenever possible as the overall visualization of target lesions for precise catheter placement is enhanced while the radiation exposure to the interventional staff is indirectly reduced. To optimize the utilization of sonography units in the daily routine, larger lesions located in the lower liver segments or caudal half of the kidney will most likely be suitable for a sonography-guided approach.

KEY POINTS

- Ultrasound-assisted catheter placement in CT-guided brachytherapy of upper abdominal malignancies significantly improves lesion visibility.
- Predictors of successful ultrasound application are larger lesions within the lower portion of liver and kidney.
- By reducing the need for CT fluoroscopy during intervention, radiation exposure to medical staff may be significantly lowered.

Conflict of Interest

The authors declare that they have no conflict of interest.

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