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ORIGINAL ARTICLE

How to operate a liver tumor you cannot see

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Abstract

Backround As recent chemotherapy regimens for metastatic colorectal cancer become more and more effective in a neoadjuvant setting before liver surgery, a "complete" clinical response is sometimes documented on imaging. Without operation though, metastatic recurrence is likely to commence within 12 months. Surgeons now face the problem to resect non-visualizable and non-palpable lesions.

Methods Computer-based virtual surgery planning can be used to fuse pre- and postchemotherapy computed tomography data to develop an operative strategy. This information is then intraoperatively transferred to the liver surface using an image-guided stereotactically navigated ultrasound dissector. This enables the surgeon to perform a resection that is otherwise not possible.

Results During operation, detection of the lesion through palpation or ultrasound was impossible. After registering the virtual operation plan into the navigation system, the planned resection was performed without problems. Histopathologic workup showed vital tumor cells in the specimen.

Conclusion The new image-guided stereotactic navigation technique combined with virtual surgery planning can solve the surgeon's dilemma and yield a successful operation.

Keywords Liver resection · CRLM · Navigation · Complete remission · Stereotactic

Introduction

The 5-year survival rates after liver resection in patients with metastatic colorectal cancer typically range between 25% and 40% [1–3]. Unfortunately, about 85% of patients with liver metastases are considered not resectable at presentation [4]. Over the last years, neoadjuvant combination chemotherapy regimens facilitated a downsizing of lesions, rendering initially irresectable metastases resectable [5]. Resection rates exceeding 20% in such patients can be achieved nowadays [6].

In cases where neoadjuvant therapy leads to a "complete" response on follow-up imaging, resection is hardly possible from a technical standpoint. As these patients tend to suffer recurrent disease in most cases in a matter of months, solving this technical problem becomes vital.

We were able to apply modern computer-assisted resection planning and navigation techniques to this technical dilemma and report the first case of a successful resection in a patient with non-visualizable, non-palpable liver metastases using image-guided surgery. To our knowledge, implementation and application of stereotactic technology explicitly dedicated to soft tissue surgery were not yet demonstrated successfully.

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Methods

Risk analysis and virtual surgery planning (MeVis)

Virtual resection planning has become an important tool (MeVis LiverAnalyzer—MeVis Research, Bremen, Germany) to plan and evaluate patient-individual-optimized surgical strategies for major hepatectomies [7, 8]. The method of acquiring data for risk stratification and intervention planning has been described elsewhere [9, 10].

In short, relevant anatomical or pathological structures such as the liver, intrahepatic vessels, and tumors are segmented (extracted) from bi- or tri-phasic computed tomography (CT) or MRI data. This allows for the calculation of patient-individual vascular territories for each vascular system and for identification of vascular branches affected by resection with certain safety margins. Resection planning can be performed in the patient-individual 3D model of the liver and modified on the original CT data as well. Analysis provides the remaining functional liver volume. Risks associated with different resection strategies can be identified and evaluated and allowed to determine an optimized individual operative strategy.

Image-guided stereotactic navigation system for liver surgery (MiMed)

The stereotactic system consists of the following components: an infrared-based optical tracking system (Vicra®, Northern Digital Inc., Canada), a navigation computer unit (PaceBlade), and a 6 degree of freedom computer mouse (Spaceball) to control the systems actions. The instruments used in stereotactic context are a linear ultrasound scanner (Terason® 8IOL, Teratech) and an ultrasound dissector (CUSA Excell, Integra Neuroscience), which are both attached with a rigid reference [11]. The system determines the spatial position and orientation of both the ultrasound probe and the dissection device in real-time (frequency 20 Hz, spatial accuracy 0.25 mm RMS) and displays this information within the virtual scene of the patient's anatomy.

Setup The navigation system is placed near the patient's head with the computer screen and the controls facing towards the surgeons. This enables the surgical team to conveniently interact with the system and interpret the systems graphical output. Throughout the course of the procedure, the 3D planning model is displayed on the screen of the navigation device together with the real-time ultrasound image.

Registration Initially, the virtual planning model is registered to the patient's anatomy. With this, anatomical landmarks in the real organ are assigned to their corresponding positions in the virtual model. Technically, for a rigid registration, at least three such landmarks are required to register the model to the patient anatomy. In reality, a precise registration requires more than three landmarks to cope for appearing deformations of the organ and changes in size and shape. We used a registration method relying on identification of vascular features as landmarks within the ultrasound images [12, 13]. In the technical workflow, corresponding ultrasound images are transferred to an additional computer and manually aligned by a member of the clinical team. The registration procedure requires a few seconds and can be repeated whenever necessary.

Navigation After the registration process, the ultrasound dissector is displayed on the computer screen within the spatial context of the virtual model. Surgical execution is facilitated by continuously displaying the position and orientation of the virtual dissector within the 3D model of the liver. This provides continuous real-time feedback to the surgeon and enables to determine whether or not the dissectors tip is close to the planned resection border or to anatomical structures of interest.

Operative procedure

The 64-year-old patient was diagnosed with cancer of the sigmoid colon in May 2007 and underwent open sigmoidectomy (T3N2M1G3). Intraoperative ultrasound showed two liver metastases (segments IV and VI), confirmed by postoperative CT scan. He received neoadjuvant leucovorin, 5-FU, and oxaliplatin (FOLFOX 4) and was referred for liver resection after three courses in November 2007. Follow-up CT showed good response—the lesion in segment VI was reduced to a 9-mm diameter while the segment IV lesion was not identifiable anymore. After registration of the ascular trees of the pre- and postchemotherapy scans, the metastases identified in the prechemotherapy scan could be fused with anatomical structures extracted from the postchemotherapy data. This allowed for calculation of risk analysis and surgery planning for both metastases although the tumor in the left medial sector was no longer visible in the current CT data. Figure 1 shows combined analysis of both CTs making resection planning possible in segment IV.

During operation, a complete examination of the liver was performed by palpation and intraoperative ultrasound. The segment VI lesion was visible and resected by wedge resection. The lesion in segment IV was neither palpable nor sonographically detectable. Therefore, the resection was performed according to the preoperatively planned strategy. This was possible by stereotactic image-guided navigation. The software displayed a 3D model of the liver anatomy,

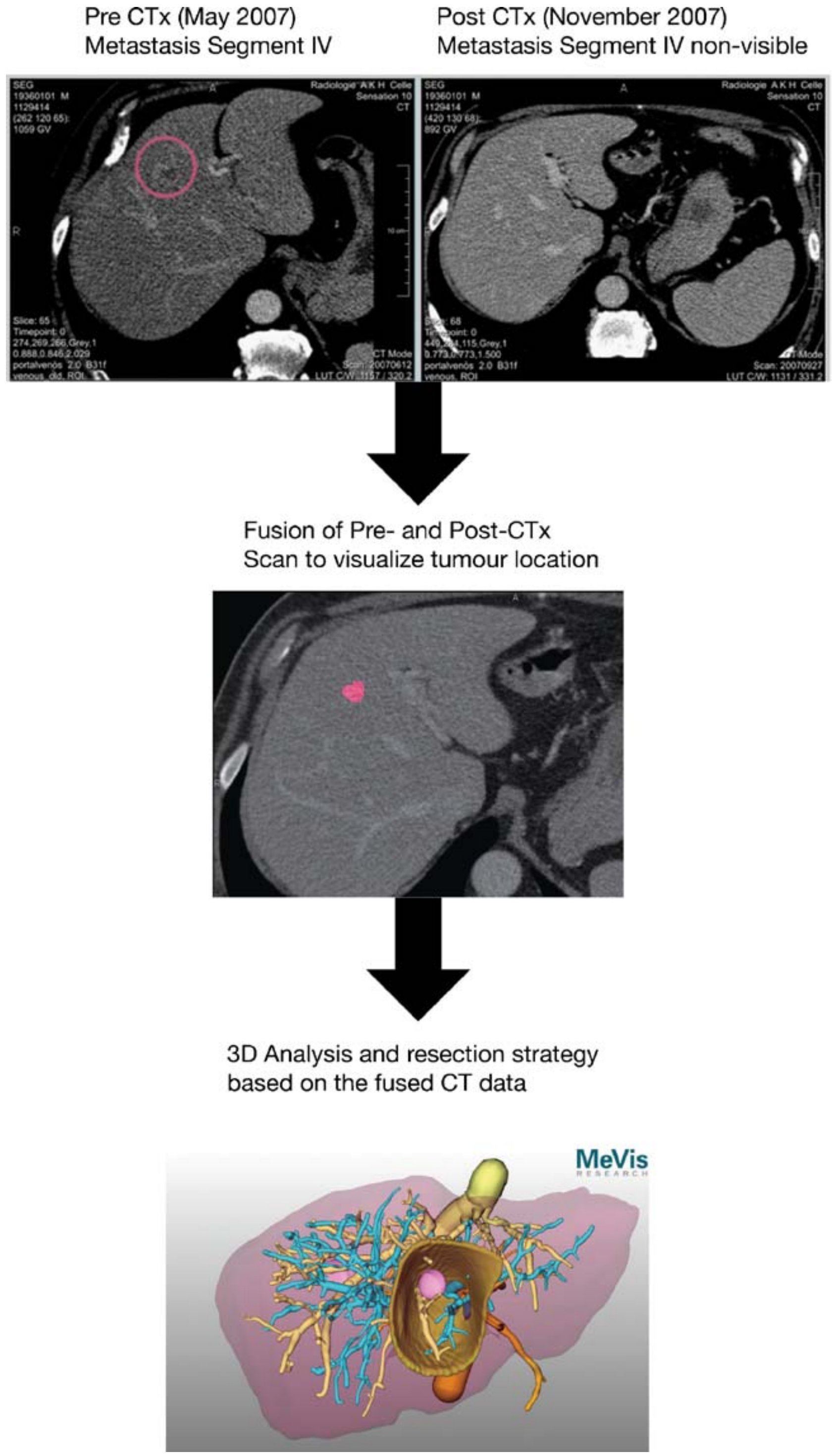

Fig. 1 Flow chart of the preoperative acquisition of planning data. Registration of vascular trees of pre- and post-chemotherapy scans enables the virtual fusion of the metastasis' location as identified in the prechemotherapy scan with anatomical structures extracted from the postchemotherapy data. The resulting overlay was used for calculation of risk analysis and surgery planning for both metastases although the tumor in the left medial sector was no longer visible in the current CT data

the resection plan, and a view of the available ultrasound images on a monitor close to the operative field.

The ultrasound transducer was placed onto the surface of the liver and a real-time ultrasound image was registered with the preoperatively generated 3D model using the 6D computer mouse by matching definable structures (e.g., portal vein and hepatic venous branches). The position of the CUSA dissector (Cavitron ultrasonic aspirator) was then registered into this image and displayed simultaneously within the 3D model of the liver. This provided continuous real-time feedback and enabled to determine whether or not the dissectors tip was following the planned resection border. The planned resection margin was strictly followed. This became more comfortable after adapting to the necessary split view between the operation site and monitor (Fig. 2). Finally, the planned resection in segment IV was completed as planned. A small tumor remnant was found in the center of the specimen. Histopathology confirmed R0 resection of vital tumor. The postoperative course was uneventful; the patient was discharged on postoperative day 7 in good general condition (Figs. 3 and 4).

Discussion

Only 10% to 20% of patients suffering from colorectal liver metastases are initially suitable for surgical resection [4]. New surgical strategies such as portal vein embolization inducing hypertrophy of the liver remnant [14, 15] and two-stage resections have been advocated to increase resectabilty in selected cases [16]. However, neoadjuvant chemotherapy is likely to have an even stronger impact.

Fig. 2 Intraoperative setup. The computer screen displaying the 3D data set with registered Instruments for online control of CUSA tip placement. The surgeons are performing the resection following the operation plan on the screen

Today, several groups have shown that neoadjuvant chemotherapy can facilitate the downsizing of colorectal liver metastases and render initially unresectable metastases resectable [4, 5]. Resection rates between 10% and 30% in patients with initially unresectable liver metastases are not unusual [5, 17]. In fact, preoperative chemotherapy is often used in clinical practice to bridge the time gap between resection of the primary tumor and metastases.

Dramatic responses described as complete clinical response on follow-up imaging have been reported after neoadjuvant chemotherapy [18, 19]. So is it really necessary to remove a metastasis after complete response? From an oncologist's view, a complete clinical response represents a good indicator for the efficacy of chemotherapy. But unfortunately the clinical response does not necessarily correlate with the pathologic response [28]. Recent data suggest that patients with complete clinical response have a high risk for either persistent disease or early recurrence [18].

Even a complete metabolic response defined as a normalization of [18F]fluoro-2-deoxy-D-glucose uptake on follow-up PET scans has been described after neoadjuvant chemotherapy [20]. Intriguingly, a recent study found that only five out of 34 lesions with complete metabolic response (15%) expressed a complete pathological response [19]. Interestingly, seven of these lesions with complete metabolic response had also disappeared on CT scans; intraoperatively, six still contained viable tumor. Thus, metastases with complete response should be removed to minimize tumor recurrence.

From the surgeon's point of view, a complete response becomes a technical dilemma because the surgeon can no longer localize the tumor for resection. But intraoperative localization of the lesion represents a prerequisite for liver resection. However, Benoist et al. [18] found macroscopic residual disease during operations in up to 24% of cases despite preoperative imaging showing a complete response. In those cases, resection can be routinely performed even if metastases are only resembled as a visible scar on intra-operative ultrasound. But how is it to resect a non-visualizable tumor and how to determine the safety margin? When the lesion can be localized to certain segments, one strategy could be to perform an anatomic resection of the segment or segments in which the tumor was previously described. But this is very theoretical and far from clinical reality because liver segments have a high inter-individual variety in volume and shape [21]. Anatomically, exact segmentectomies are difficult to perform and only possible by the help of vascular occlusion or dye infusion techniques of segmental vessels [22].

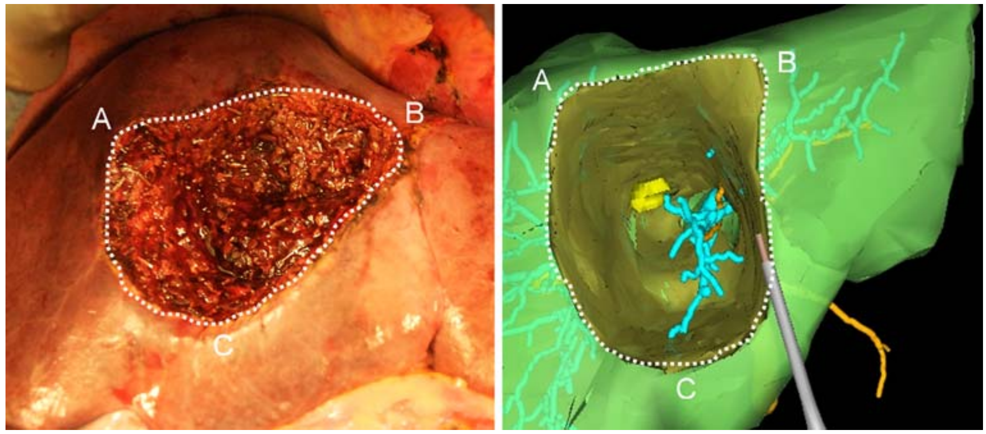

Fig. 3 The resection surface is matched with the navigated operation plan from the monitor

If the surgeon could target the lesion within the liver with a higher degree of accuracy, it could lead to smaller resections, tumor-free margins, and therefore, improved outcomes. Since image-guided surgery has been shown to provide navigational assistance to the surgeon by displaying the surgical probe position on preoperative imaging in almost real time, the technology was applied to overcome this clinical problem. In general, image-guided navigation technology is already used with good results in neurosurgery, otolaryngology, and orthopedic surgery. However, the use of this technology in mobile and deformable abdominal organs like in the liver with its translational motion due to respiration is more complex. The main problem is to obtain precise registration of fixed pre-treatment image data sets with continuously changing patient anatomy.

To our knowledge, only a few groups have tried to implement stereotactic systems for soft tissue surgery. But only general applicability [23, 24] or algorithmic solutions [25, 26] could be demonstrated so far. Reliable, precise, and applicable soft tissue registration procedures are not available yet, but some experimental approaches are described that still lack clinical application and validation [27]. Combining 3D CT data with intraoperative ultrasound allowed for a reliable registration process in our study, but the localization of the tumor in the median sector of the liver meant very little mobilization.

In order to further improve the precision and reproducibility of the system and the therapeutic approach, further developments of the registration process are imperative. An extended ultrasound image analysis towards an automated vessel tree registration procedure is an interesting approach but its achievement with the currently available ultrasound quality and available computing power seems rather challenging. The future goal is to provide a system with optimal integration of such technology in the clinical workflow. Using novel technology should not increase surgery time nor should it alter clinical workflows unnecessarily.

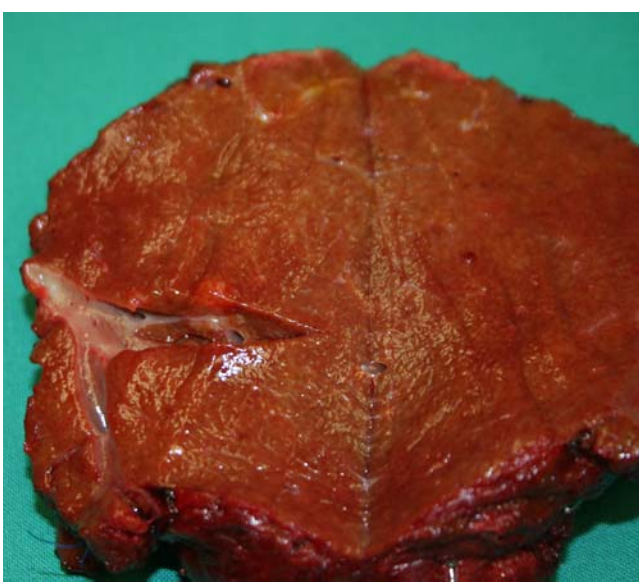

Fig. 4 Resection specimen, separated in the middle. The small tumor is now visible in the expected position

Summary

In this case, we were able to demonstrate the potential of this technology for solving the dilemma of resection of a non-visualizable and non-palpable tumor. In our view, tumors in segment IV and eventually in segments V and VIII are good candidates for this technique because resection can be performed without major anatomic shifting or deformation of the liver.

In summary, a successful R0 resection of a “disappeared” metastasis was performed by using image-guided stereotactic liver resection, which has been demonstrated for the first time in such a case to the authors knowledge. With increasing use of neoadjuvant chemotherapy in patients suffering from colorectal liver metastases, the problem of non-visualizable and non-palpable tumors will increase providing an ideal indication for image-guided navigation technology.

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