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Ex vivo magnetic resonance imaging of pretransplant human donor liver

Clinical experience in 66 cases

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Abstract Magnetic resonance imaging (MRI) was performed on 66 cold-stored human donor livers. Spin echo images were obtained with a clinical whole body MRI system. Various parenchymal and vascular abnormalities were found. An unexpected finding was the abundant presence of intrahepatic air. Although the majority of parenchymal abnormalities that were found would not have precluded transplantation, the rationale of pretransplant MRI was to prevent the introduction of unidentified pathology into the recipient. Guided by the MR images, lesions in the isolated organ can be easily located for biopsy and resection. Unnecessary or inadequate therapeutic interventions after transplantation can thus be avoided. In addition, the visualization of the hepatic veins with their confluence appears to be useful in split-liver procedures.

Key words *Liver transplantation*, MRI · MRI, pretransplant, liver Pretransplant, liver, MRI

Introduction

The assessment of donor organs in clinical practice is presently based on clinical and biochemical parameters, e.g., medical history, drugs, standard liver function tests, and circulatory status [12]. In the vast majority of potential liver donors, no special radiographic evaluation of the transplantable abdominal organs is employed. Furthermore, inspection and palpation of the explanted isolated organs is known to be inaccurate. Therefore, after explantation, information about parenchyma and vasculature of a human donor liver can be obtained only through invasive techniques such as biopsy and injection of contrast fluid. These techniques endanger the integrity of the organ. However, when these techniques are not applied, the liver is not checked for structural abnormalities that may prohibit transplantation.

A completely noninvasive technique that is particularly suited to the visualization of parenchymal tissues and vessels is magnetic resonance imaging (MRI). Although MRI systems have been used for spectroscopy of isolated donor organs [16], the clinical feasibility of pretransplant imaging has not been evaluated. Yet, there is potential for wide application of this since nowadays all transplant centres have MRI facilities available; some of them even have scanning systems in the operating rooms.

The aim of the present study was to investigate whether MRI could detect abnormalities of parenchyma and vasculature of the pretransplant human donor liver. In addition, we investigated whether MRI could display the liver vasculature and, if so, whether such information could be helpful in the preparation of split-liver grafts for transplantation.

Materials and methods

Donor livers

Sixty-six human donor livers were included in the study. Livers were harvested from brain-dead, hemodynamically stable donors according to a standardized operative procedure [13]. In this procedure the liver was flushed in situ with 2 l University of Wisconsin (UW) solution (Universtiy of Wisconsin, DuPont Critical Care, Waukegan, Ill., USA) via the aorta and the portal vein. After the liver was removed from the body, an additional flush through the hepatic artery and biliary system was performed with UW solution until the outflow from

Table 1 MRI findings in 66 human donor livers

Donor livers	Accepted $n = 57$	Discarded $n = 9$
No parenchymal abnormalities and no intrahepatic air	22 (39%)	2 (22%)
Parenchymal abnormalities	6 (10%)	2 (22%)
Minor intrahepatic air	21 (37%)	3 (33%)
Major intrahepatic air	8 (14%)	2 (22%)

the caval vein was clear. Livers were then stored, floating in UW solution, in sterile plastic bags on melting ice in styrofoam containers until the time of transplantation. Fifty-six of the 57 livers accepted were subsequently transplanted. One initially accepted liver was discarded later. Nine discarded livers were also included in the study. Reasons for discarding them included suspicion of malignancy, previous hypotensive periods in the donor ($n = 3$), alcohol ($n = 1$) or drug ($n = 1$) abuse in the donor, hepatic artery aneurysm ($n = 1$), improper cold perfusion ($n = 1$), recent streptokinase therapy ($n = 1$), and cystic liver disease ($n = 1$).

MRI

Images were obtained with a 1.5 Tesla whole body MRI system (Philips Gyroscan S15/HP, Philips Medical Systems, Best, The Netherlands) with a standard body coil.

Imaging protocol

All imaging was performed before the start of the recipient operation. To guard against leftover metal surgical instruments entering the magnetic field unintentionally, the donor liver in its full package was checked with a metal detector (Binger, type 610, Germany). Then, to optimize image quality, the container with the liver was positioned in the isocenter of the magnet. Since changes in the amount of water from the melting ice that surrounds the plastic storage bags during the measurement can alter the load of the coil and can, thereby, affect image quality, melting water was continuously removed by a suction cannula located on the bottom of the styrofoam container and connected with a vacuum system. The plastic bags themselves were never opened, so that the livers remained sterile within their original packages. Scoutview images allowed us to determine the exact position of the liver in the container and also allowed us to plan subsequent imaging series.

Instrumental settings

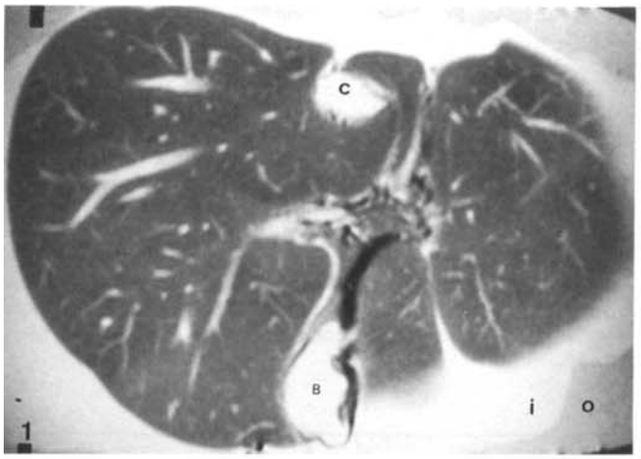
For a proper visualization of the parenchyma of a donor liver that is stored on ice, the conventional parameter settings used for in vivo in situ imaging of the liver cannot be used. The reasons are, first, that the UW solution that is used for perfusion contains raffinose, branched hydroxyethyl starch, lactobionic acid, and many other substances. This induces resonance characteristics that are essentiall different from in vivo in situ liver imaging. Second, the low temperature used for organ storage (0°C) also has its effects on the resonance characteristics of the liver. For these two reasons, MR parameter settings must be adjusted for imaging cold-stored organs. In a separate study the results of which are not discussed here, we determined the optimal parameter settings necessary for the visualization of parenchyma and vasculature of UW solution-perfused donor livers that are stored on ice. For the visualization of liver parenchyma, moderately T_1-weighted spin echo pulse sequences with a repetition time of 800–1200 ms were used. The echo time was set to 20 ms. The slice thickness ranged from 3 to 5 mm. To selectively visualize the liver vasculature by enhancing the distribution of UW solution, moderately T_2-weighted spin echo pulse sequences with a repetition time of 1000 ms and an echo time of 80 ms were used. A maximum contrast between UW solution and liver parenchyma was obtained with these parameter settings. This method visualized vascular structures without the use of contrast agents. To capture the large-caliber hepatic vessels, a large slice thickness must be used, 25–35 mm, depending on the size of the liver. For a better depiction of the vascular structures, gray scale inversion was used in these images. All images were printed with a Scopix Compact system (Agfa-Gevaert, Germany).

Results

The results are summarized in Table 1. MRI showed morphologically normal liver parenchyma with only minor regional differences in resonance characteristics and proper filling of the hepatic vessels with UW solution in 22 of the 57 accepted livers and in 2 of the 9 discarded livers (Fig. 1).

Air collections in the intrahepatic vasculature were found in 29 of the 57 accepted livers and in 2 of the 9 discarded livers. In these cases, no other parenchymal abnormalities and no major regional differences in resonance characteristics in liver parenchyma were observed. The amount of air ranged from some minor bubbles in the central parts of the hepatic and/or portal veins (21 of the 57 accepted livers, 3 of the 9 discarded livers) to major peripheral accumulations of air, predominantly in the right liver lobe (8 of the 57 accepted livers, 2 of the 9 discarded livers; Fig. 2). In two livers in the accepted group, air was also found concomitantly in the hepatic artery branches. Air tended to be located in the upper parts of the liver. One discarded liver showed air in almost all peripheral venous and arterial branches.

Parenchymal abnormalities were present in six accepted livers and in two discarded livers. In one case where ultrasound of the liver donor had not shown any parenchymal abnormalities, two hypointense areas, $3 \times 3 \times 1$ cm and $1 \times 1 \times 1$ cm, respectively, were detected in the left lobe (Fig. 3). Hematomas or vascular malformations were suspected, but malignancy could not be excluded. Therefore, a resection of segments II and III was performed. The reduced-size liver was successfully transplanted. Histology of the resected segments showed that the lesions consisted of hematomas. In another case, MRI demonstrated the impossibility of performing a reduced-size liver transplantation. In this case, a nodule was found in the left side of the liver on palpation during hepatectomy. A needle biopsy showed focal nodular hyperplasia, and a reduced-size transplantation of the right part of the liver was proposed. However, MRI showed similar multiple lesions in the right side of the liver as well. The liver was subsequently discarded. Histology showed the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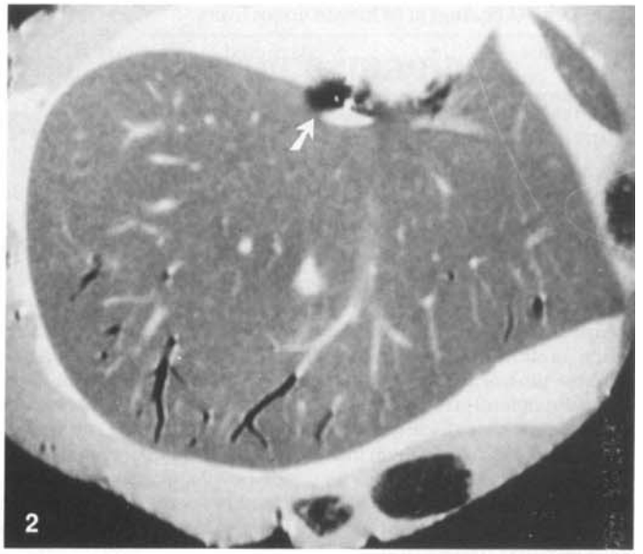
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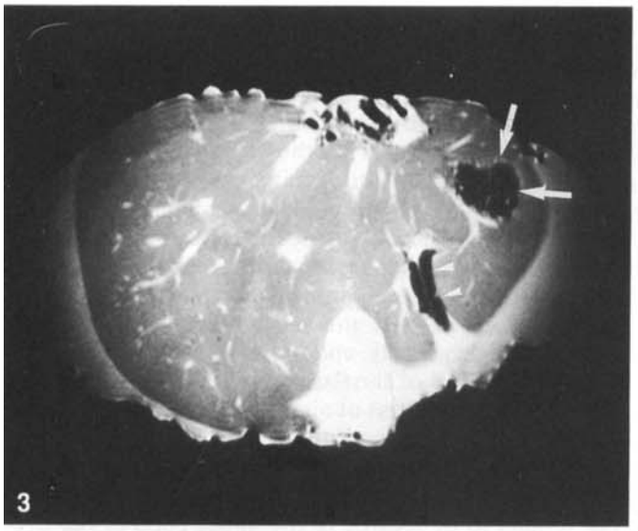
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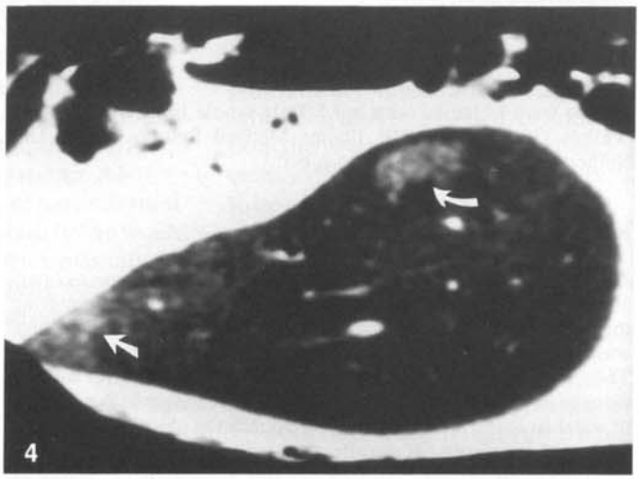
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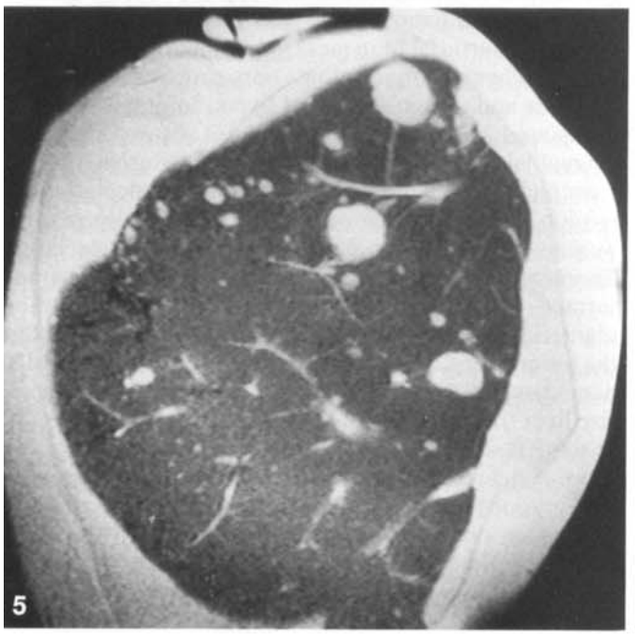
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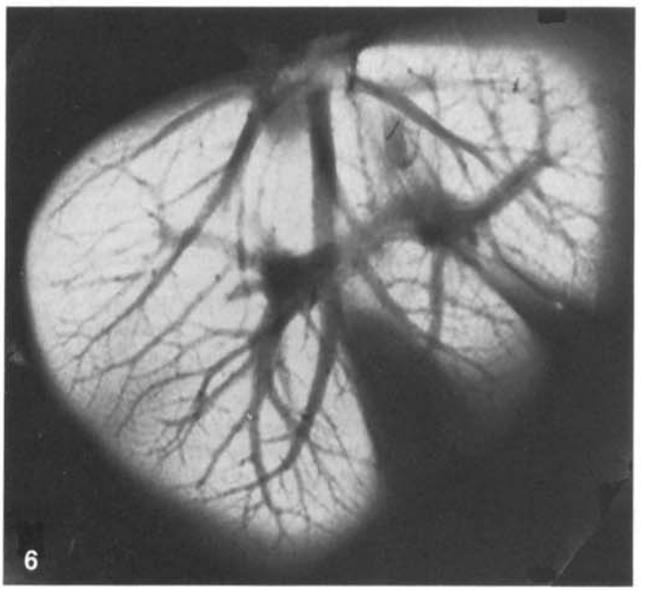
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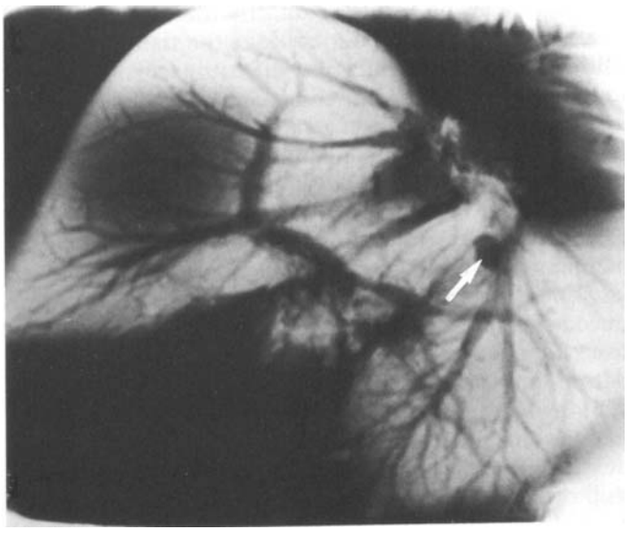

Fig. 7. "Thick slice" image demonstrating a hemangioma *(arrow)* medial of the left hepatic vein. Coronal image: TR 1000 ms, TE 80 ms, slice thickness 30 mm (gray scale reversal)

Fig. 1 Coronal image with the typical appearance of a normal donor liver. The right and left liver lobes as well as the lobus quadratus and the lobus caudatus can be seen. Hepatic and portal vein branches and the inferior caval vein *(c)* are visible. The vessels are filled with UW solution and they have the same signal intensity as the UW solution in the inner plastic bag *(i)*. The outer plastic bag *(o)* contains saline that has a longer T_1 and a longer T_2 than UW solution. The gall bladder *(B)* has been opened and is filled with UW solution. TR 1000 ms, TE 20 ms, slice thickness 3 mm

Fig. 2 A branching pattern of air up to the edge of the liver. The black spots in the outer plastic bag are ice cubes. A signal void due to a surgical clip *(arrow)* is present at the orifice of the inferior caval vein. Coronal image: TR 1000 ms, TE 20 ms, slice thickness 3 mm

Fig. 3 A hematoma in the left liver lobe *(arrows)*. Air is visible in the ligamentum teres hepatis *(arrowheads)*. The lesion has irregular margins and is not filled with UW solution. The other hematoma is not visible in this slice. Coronal image: TR 1000 ms, TE 20 ms, slice thickness 3 mm

Fig. 4 Patchy areas with irregular margins suspect for focal fatty infiltration *(arrows)*. Level and window settings are adjusted to enable distinction of the lesions from the surrounding normal liver parenchyma. Transverse image: TR 800 ms, TE 20 ms, slice thickness 3 mm

Fig. 5 Discarded donor liver showing numerous cysts of different size and shape. Coronal image: TR 1000 ms, TE 20kms, slice thickness 3 mm

Fig. 6 "Thick slice" image showing the right, middle, and left hepatic veins and their confluence. The UW solution filled gallbladder is also visible, as are the main branches of the portal vein. Coronal image: TR 1000 ms, TE 80 ms, slice thickness 30 mm (gray scale reversal)

multiple lesions to be focal nodular hyperplasia. Three livers showed multiple patchy areas of increased signal intensity on moderately T_1-weighted images (Fig. 4). With more T_2 weighting of the images, the lesions became isointense. The anatomical distribution and the resonance characteristics of these lesions had the MRI appearance of focal fatty infiltration [6], but we have no histology to confirm this. Since focal fatty infiltration does not preclude transplantation, these three livers were transplanted and no major organ dysfunction was observed after transplantation. In one discarded liver, MRI revealed cysts throughout the entire liver (Fig. 5). Cystic liver disease was confirmed by histology. In one case, the MRI of a liver destined for bipartition showed three parenchymal lesions. One of the lesions appeared to be close to a hepatic vein. Because of this and the fact that the lesions had the same signal characteristics as the UW solution in the vessels, hemangiomas were suspected. The liver was split into two parts for split-liver transplantation. During the transection we found evidence of two hemangiomas by visual inspection. The third hemangioma was removed together with segment IV in the splitting procedure. The diagnosis was confirmed by histology. Ultrasound imaging in one of the recipients clearly showed the hemangiomas in the graft. Because the presence and the localization of the lesions were known from the MR images, no further diagnostic action had to be undertaken. With moderately T_2-weighted imaging, information could be obtained about the distribution of UW solution through the graft, i. e. depicting the UW solution filled vascular structures in the liver. Accurate positioning of a single 30-mm-thick T_2-weighted slice resulted in a clear depiction of the large hepatic veins and their confluence in particular (Fig. 6). The variable entrance of the middle hepatic vein in the inferior caval vein could clearly be visualized. The information about the hepatic venous architecture was useful in planning the bipartition of eight donor livers. For six split-liver transplantations and for two reduced size transplantations. For example, in the liver containing hemangiomas mentioned earlier, workbench arteriography before the split procedure failed to detect the lesions. The „thick slice" T_2 images clearly showed the localization of the hemangioma and its relationship to the main branch of the middle hepatic vein (Fig. 7). Due to their curved course, which made them hard to capture within one plane, the anatomy of the portal and arterial vessels in their common vascular sheath was hard to visualize.

Discussion

This study shows that MRI can be used for the detection of abnormalities in parenchyma and vasculature of pretransplant human donor livers. In addition, selective imaging of the hepatic veins without using contrast fluid was possible and appeared to be helpful in split-liver procedures.

An unexpected finding was the abundant presence of intrahepatic air collections with no other associated abnormalities. Air was observed mostly in the central hepatic veins where it may have been introduced during donor hepatectomy after in situ perfusion; when the large veins are cut, regurgitation of air into the proximal part of the vessels occurs. Air in portal vein and hepatic artery branches was observed less frequently and may have been introduced by leaking perfusion catheters during in situ hypothermic perfusion or during subsequent workbench procedures. In portal venous air, the predominant location in the right liver lobe may reflect the preference of air bubbles to enter the right portal vein since, during the workbench procedure, its direction is slightly more upward than that of the left portal vein. Although it was demonstrated that air can have serious consequences for organ preservation procedures by impeding the entry of preservation solution into the vessels [14], the effects of the air collections on the transplant procedures are not yet clear. In two cases of proven portal venous air, an unequal vascular refill pattern with cyanotic spotty discoloration during portal reperfusion was observed. This may have been caused by a temporary obstruction of the blood flow due to air embolism. The liver regained its normal color after some time. The effect of air collections on post-transplant organ function, if any, is a subject for further research.

From hepatic artery embolization procedures it is known that gas bubbles can stay in the portal venous system for as long as 8 days [8]. Therefore, it is not merely hypothetical that some air can remain in the liver after transplantation. Although not demonstrated in our study, the presence of such air could be mistaken for conditions like gas gangrene and could lead to unwanted or inadequate interventions [3–5]. Demonstration of air in the liver before implantation can prevent such a misdiagnosis.

A homogeneous signal intensity of liver parenchyma, as was observed in most livers, probably indicates a homogeneous distribution of UW solution throughout the entire liver. The effectiveness of the in situ perfusion might thus be evaluated with MRI.

The ability of MRI to visualize the vessels of isolated donor livers was clearly demonstrated in the „thick slice", T_2-weighted images. In contrast to magnetic resonance angiography (MRA) studies of in situ renal grafts in which the flowing blood is „magnetically highlighted" [2], we used the stationary UW solution in the vessels as a „natural" contrast agent. The high content of branched hydroxyethyl starch and other macromolecules make UW solution an excellent contrast agent for both T_1- and T_2-weighted imaging. Although the variable entrance of the middle hepatic vein in the inferior caval vein can be indicated by inspection of the orifices from inside the cava on the bench, this is only possible once the liver has been taken out of the plastic bags. MRI can provide the same information with a slight logistic advantage since the information can be available shortly after arrival of the organ, usually several hours prior to the start of the splitting operation. The availability of anatomical information at that point still allows modifications of the splitting procedure. The identification of large branches of the middle hepatic vein crossing the main hepatic fissure to the right side may also be clinically relevant. The demonstration of such veins can indicate the necessity of conservation of the middle hepatic vein for the preparation of the right graft. This may also imply discarding segment IV as part of the left-sided graft [7]. In split-liver procedures and in reduced-size liver transplantations, the information mentioned about the hepatic venous architecture is relevant in determining the choice of the transection plane during the splitting procedure [9, 10, 15]. Since vascular abnormalities are filled with UW solution, they can easily be detected in „thick slice" T_2 images. The spatial relationship of the malformations with the vascular architecture can be determined and this information can be used in bipartition procedures.

In seven of the nine discarded livers, MRI could not detect parenchymal abnormalities. The underlying cause for discarding them was probably found at the biochemical or ultrastructural level, but was not detectable with MRI as employed in this study.

For imaging cold-stored donor organs, MRI has several advantages over other imaging modalities like computed tomography and specimen ultrasound. The most important advantage of MRI is that the liver remains in its original package, stored on crushed ice. Because there is no need to use contrast agents, there is neither an increased risk of microbial contamination nor a risk of warming the organ. The absence of radiation exposure and the easy positioning of imaging planes, as opposed to the need to move the object, is another advantage of MRI. It could be argued that specimen ultrasound can provide the same information as MRI, but we found that the sound waves cannot penetrate the plastic bags that surround the liver. Specimen ultrasound with the transducer placed directly on the liver surface may be valuable, but the sterility of the organ becomes endangered. We have no experience with this technique. Nowadays, MRI facilities are available at all transplant centers; some of them even have scanning systems in the operating rooms. Therefore, MRI is preferable for imaging cold-stored donor livers.

It was demonstrated that MRI can detect a variety of parenchymal abnormalities. The majority of these abnormalities were benign and would not have precluded transplantation. However, in the case of the hematoma and the hemangioma, as well as in the case of focal nodular hyperplasia, MRI detected lesions that had escaped the palpating fingers of the surgeons. Moreover, well-known diagnostic imaging techniques like ultrasound and workbench arteriography had also failed to detect these lesions. MRI, used as an additional quality check of the organ before transplantation, was able to detect these le-

sions. This informatioon directly affected the surgical approach to the transplantation. Guided by the MR images, the lesions in the isolated organ were easily located for biopsy and resection. Clinically important lesions are not necessarily „pathological" (hematomas, hemangiomas); they also include „benign" lesions (focal fatty infiltration, adenomas, solitary cysts). When detected in imaging studies after transplantation, such unknown lesions can be misinterpreted and can lead to unnecessary or inadequate therapeutic interventions. The rationale of pretransplant MRI could, therefore, be that it can prevent the introduction of unidentified lesions into the recipient [1, 11].

Although, in the future, the increasing availability and the development of faster scanning systems may make MRI cheaper, MRI scanning time is now relatively expensive. This is one reason to keep the examination as short as possible. Another reason to keep scanning time to a minimum is that the transplant procedure does not allow for much delay. The short routine imaging session, as we have been using it in liver transplantation for 2 years, consists of scoutview imaging followed by imaging of the entire liver in 25–30,3-mm-thick slices with a Repetition time of 800–1200 ms and a Echo time of 20 ms. This entire investigation takes less than 10 min of scanning time. In the case of split or reduced-size liver transplantation, additional „thick slice" imaging of the hepatic veins is possible in a few extra minutes of scanning time. MRI can be performed shortly after arrival of the donor liver in the transplanting hospital. This enables availability of the anatomical information at an early stage of the transplantation, when surgical procedures and transplantation logistics still can be changed.

In summary, we conclude that MRI is a fast, safe, and noninvasive method to study parenchyma and vasculature of the pretransplant human donor liver with minimal interference in the transplant procedure. A short pretransplant MRI session can detect lesions with potentially clinical consequences. The hepatic veins with their confluence can easily be visualized, thus allowing the planning of liver-splitting procedures.

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