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Review

Contribution of Computed Tomographic Angiography to Pretreatment Planning of Radio-embolization of Liver Tumors

HYNEK MIRKA[1,2], PETR DURAS[1], JAN BAXA[1], EVA KORCAKOVA[1,2] and JIRI FERDA[1]

[1]*Department of Imaging Methods, Faculty of Medicine in Pilsen, Charles University in Prague and Teaching Hospital, Pilsen, Czech Republic;*
[2]*Biomedical Centre, Faculty of Medicine in Pilsen, Charles University in Prague, Pilsen, Czech Republic*

Abstract. *Transarterial radio-embolization (TARE) using yttrium-90 microspheres is a promising method based on the brachytherapeutic effect of radionuclide with beta-minus decay dissolved in solid microparticles applied directly to tumor-supplying arteries. This treatment is complex, as well as logistically and technically extremely demanding and must be planned in detail. The visualization of the vascular supply of the liver and the possible parasitic supply of the tumor is essential not only for indication of the procedure and correct identification of the arteries to which the microspheres will be applied, but also for prevention of non-target deposition of radioactive material. This review addresses the use of computed tomographic angiography in the preparatory phase of TARE.*

Locoregional treatment is currently an important part of comprehensive care for patients with liver tumors. Specifically, it is indicated in patients with primary and secondary malignancies who are not suitable candidates for liver resection or transplantation. Standard methods used in this area are thermal ablation (radiofrequency ablation, microwave ablation or cryo-ablation) and intra-arterial treatment (TACE) (1). Transarterial radio-embolization (TARE) using yttrium-90-containing glass or resin microspheres is a promising new method based on the brachytherapeutic effect of radionuclide particles applied directly to the tumor-supplying arteries (2). This treatment is complex, as well as logistically and technically extremely demanding, and must be planned in detail. Therefore, the anatomical and functional parameters of the liver and its circulation are assessed in a multimodal manner using radiological and nuclear medicine methods. The visualization of the vascular supply of the liver and the possible parasitic supply of the tumor is essential, not only for indication of the procedure and correct identification of the arteries to which the microparticles will be applied, but also for prevention of non-target deposition of radioactive material (3). This review addresses the use of imaging methods in mapping of the liver arterial anatomy in the preparatory phase of TARE.

Correspondence to: Associate Professor Hynek Mírka, MD, Ph.D., Department of Radiology, Medical School and Teaching Hospital Pilsen, Charles University in Prague, Alej Svobody 80, 304 60 Plzen, Czech Republic. Tel: +420 377103456, Fax: +420 377103438, e-mail: mirka@fnplzen.cz

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Arterial Supply of the Liver and its Importance in TARE

The complex embryonal development of the hepatobiliary system predisposes this area to having a highly variable arterial anatomy (4). A classic arrangement with two hepatic arteries arising from the proper hepatic artery, which is a branch of the common hepatic artery arising from the *truncus coeliacus*, occurs in 50-61% of individuals (5-7). In other cases, the arteries are replaced, or accessory arteries are found (Figure 1). According to Michels' classification, 10 types of arterial variants exist (Table I) (8). The arteries that supply the surrounding organs can also originate from hepatic arteries. For example, the right gastric artery, accessory left hepatic artery, lower diaphragmatic artery and umbilical artery may be branches of the left hepatic artery (9). An examination of liver segment IV should be focused on the possible presence of the middle hepatic artery, which may be a branch of the right hepatic artery or arise directly from the proper hepatic artery as a trifurcation with the end branches of the right or left hepatic artery passing on the other side. Moreover, mapping the distance of normal arterial branches from the point of microsphere application is also important,

Table I. *Anatomic variants of hepatic arteries (8).*

Michels type	Description	Occurrence
I	Normal anatomy	55-61%
II	Replaced LHA	3-10%
III	Replaced RHA	8-11%
IV	Replaced RHA and LHA	1%
V	Accessory LHA	8-11%
VI	Accessory RHA	1.5-7%
VII	Accessory RHA and LHA	1%
VIII	Replaced RHA and accessory LHA or accessory RHA and replaced LHA	2.5%
IX	CHA replaced to SMA	2-4.5%
X	CHA replaced to LGA	0.5%
Unclassified	CHA arising from aorta	2%
	Double hepatic artery Replaced PHA	4%
	Others	<0.5%

LHA: Left hepatic artery; RHA: right hepatic artery; CHA: common hepatic artery; SMA: superior mesenteric artery; LGA: left gastric artery; PHA: proper hepatic artery.

Table II. *Extrahepatic collaterals supplying liver tumors (9).*

Location of the tumor	Possible sources of parasitic arteries
Bare area of the liver	Right phrenic, right adrenal artery
Superior-anterior part	Right internal mammary artery
Exophytic toward kidney	Right renal, right adrenal artery
Any periotoneal surface	Omental branches of RGA
Near chest wall	Lower intercostal artery
Left lateral segment	Left gastric artery
Near colon	Colic branches of SMA
Gallbladder fossa	Gastic artery

RGA: Right gastric artery; SMA: superior mesenteric artery.

especially for the gastroduodenal and cystic arteries (10). Specifically, up to 17% of tumors located on the liver surface have a parasitic arterial supply (Table II) (11).

Non-target radiopharmaceutical deposition may cause serious complications, such as cholecystitis, gastrointestinal ulceration or bleeding, gastritis, duodenitis, pancreatitis, hepatitis, supra-umbilical dermatitis and radiation pneumonitis (12-14). Therefore, all patients undergo protective embolization of the gastroduodenal artery, left gastric artery, cystic artery or other arteries which may allow the non-target deposition of microspheres (15, 16). To ensure the redistribution of blood in the liver, individual branches supplying liver tissue may be embolized in some patients. Other adverse factors that increase the probability of embolization in non-target areas are stenoses and the slowing of flow in the hepatic arteries. Proper catheter positioning based on the knowledge of the liver arterial architecture is essential in order to perform the evaluation of liver perfusion and assessment of hepatopulmonary fraction deposition of microspheres before TARE. Hepatopulmonary shunting is evaluated with single photon-emission computed tomography/computed tomography (SPECT/CT) using technetium-99 m-labelled human albumin macro-aggregate in order to assess the potential radiation injury, occurring when the arteriovenous shunting exceeds more than one-tenth of the applied activity.

Imaging of portal venous system is also very important in the planning of TARE. Portal vein thrombosis with the absence of hepatopetal flow increases the likelihood of ischemic involvement of the liver and is a contraindication for TARE using resin microspheres. The procedure with glass microspheres can be successfully performed in this condition (17).

Methods of Liver Artery Imaging

Based on the above, the Imaging of liver artery variants and the parasitic supply is necessary in order to optimize the effect of TARE. To this end, the gold standard method is digital subtraction angiography (DSA). DSA consists of the non-selective imaging of the abdominal aorta, the selective imaging of the coeliac axis and superior mesenteric artery, and the super-selective imaging of all arteries that supply the hepatic parenchyma. In addition to the right and left hepatic arteries, the cystic artery, supraduodenal, retroduodenal, falciform, left gastric accessory, and right and left inferior phrenic arteries should also be located. Angiography may be supplemented with cone-beam CT which, contrary to multi-detector CT, uses a two-dimensional detector. From the data obtained, three-dimensional images showing not only the anatomy of the arteries but also the tumor tissue can be reconstructed. Cone-beam CT use in hepatic interventional radiology thus enables more selective catheterization and increased treatment efficacy. The diagnostic part of the procedure may be followed by protective embolization using metallic spirals or tissue glue of arteries that might allow the non-target deposition of microspheres.

Moreover, CT or positron-emission tomography (PET)/CT images of the liver including a series of thin slices in the arterial and venous phase are a common part of liver tumor staging. Specifically, performing the CT scan on a multi-detector scanner (optimally with 64 or more detector rows) allows a fairly detailed assessment of vascularity, but hepatic artery imaging can also be performed using magnetic resonance imaging (MRI) (18).

Technique of CT Angiography (CTA)

CT images of the liver are obtained after the injection of contrast medium (CM) in the arterial, venous and, optionally, equilibrium phases. The volume of CM should correspond to 500-600 mgI per kilogram of body weight, and the iodine flux should be in the range of 1.6-2.0 g/s. CM injection is

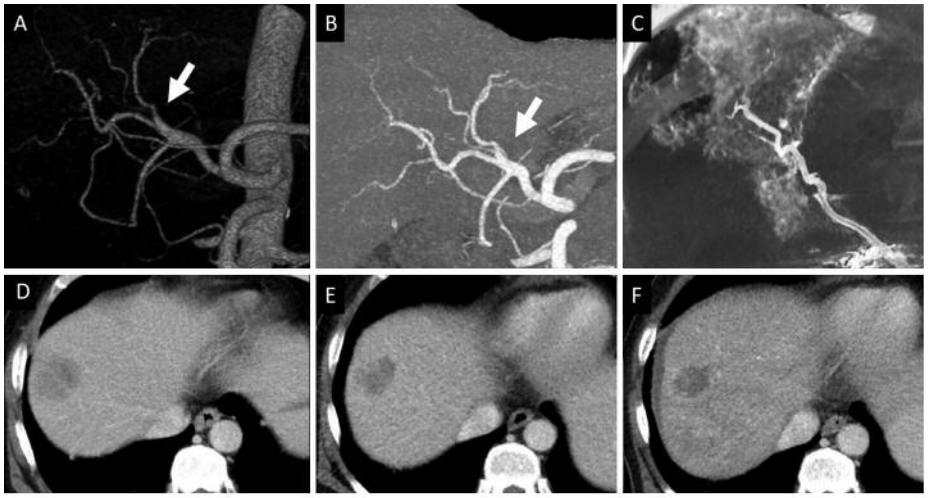

Figure 1. *Computed tomography angiography (CTA) of the liver showing the intrahepatic segmentation of the hepatic artery. A trifurcation of the hepatic artery (arrow) is visible. The supplementary artery supplies the gall bladder and part of the metastasis. A: CTA, volume-rendered 3D reconstruction. B: CTA, maximum intensity projection of hepatic arteries. C: Catheter-based perfusion image from cone-beam CT. D: Axial CT image of liver metastasis before transarterial radio-embolisation (TARE). E: Axial CT image 6 weeks after TARE. F: Axial CT image 6 months after TARE, with visible size reduction and decrease in density representing necrosis.*

followed by a saline flush to ensure high-quality visualization of both the arterial and venous system, the liver parenchyma, and possible focal lesions (19). In order to increase the contrast between the vessels and structures of the gastrointestinal tract, the per-oral application of water or mannitol water solution is advisable. Moreover, if the examination is performed only to map the liver artery, the volume of CM can be reduced by approximately 20% (20).

The early arterial phase (15-20 s after the start of CM injection or immediately after reaching a threshold of 100 HU in the aorta) is recommended for arterial imaging. At this stage, the concentration of CM is sufficient in the arteries but not in the portal vein and hypervascular lesions, which are not yet enhanced. Therefore, the signal-to-noise ratio is higher between the vessels and surrounding structures, which simplifies the visualization of small arteries. However, liver tumors should be imaged in the late arterial phase (approximately 35-40 s after the start of the contrast medium injection or 15-20 s after reaching a threshold of 100 HU in the aorta). At this phase, the portal vein and hypervascular liver lesions are enhanced, which results in a lower signal-to-noise ratio. However, in a study to compare the benefits of early and late arterial phase examinations of liver arterial variants, Van den Hoven *et al*. showed that liver arterial imaging did not produce significantly worse results in the late arterial phase than the early arterial phase (21).

In non-obese patients, the low-voltage (80-100 kV) technique is preferred in because it increases the CM contrast and consequently increases the resolution of blood vessels and hypervascular focal lesions at a lower radiation dose (22). Depending on the voltage drop, the current must be increased to optimize image quality, and the ratio of contrast to noise is not significantly reduced under these conditions (23). To optimize the exposure parameters, automatic kVp setting and automatic off-line and on-line current modulation systems are currently used. Alternatively, image noise and radiation load can also be reduced using iterative reconstructions.

Scanning on multi-detector devices is performed using submillimetric collimation (typically 0.5-0.75 mm), which ensures an isotropic data field that allows multiplanar reformations and three-dimensional reconstructions in any plane without a loss of resolution. To increase spatial resolution, some authors recommend the use of the edge-enhancement reconstruction algorithm (24). Thin axial sections and multiplanar reformations or maximum intensity projection reconstructions are used for evaluation (25).

The Importance of CTA

CTA provides sufficient time and spatial resolution for replacing diagnostic angiography in clinical practice. Optimally performed examinations can detect arterial branches with a diameter of 1 mm, and visualizing the hepatic arteries with proximal widths between 2-3 mm is usually sufficient (26, 27). Comparative studies of the accuracy of CTA and other methods (DSA, cone-beam CT) indicate that DSA is more accurate when detecting liver

arterial anomalies, especially in the area of the right hepatic artery (detectable at 65% CTA). However, the authors of these studies also agree that CTA accurately assesses the supply of the fourth hepatic segment (up to 36% higher detecability than with DSA) (21, 28, 29). Similarly, good results were obtained in the detection of the falciform artery – Burgman *et al*. detected this artery in 4.5 as many patients when using CTA compared with DSA (52.3 *vs*. 11.9%) (29). MRI, alone or as a part of PET/MRI, is another commonly used method for detection, differential diagnosis and staging of liver tumors. As with CT, liver artery anatomy can be evaluated in images obtained in the arterial phase. However, this method is less accurate than CTA; one study showed that the reliability of MRI was lower than that of CTA, especially in the area of the left hepatic artery (18).

Despite the limitations associated with CTA, it can be considered a suitable method for planning the catheterization procedure. Specifically, it accelerates and consequently reduces the radiation load and the amount of CM required, which is beneficial, especially for patients with impaired renal function (10, 21, 28).

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