Liver-Directed Interventional Oncology: My Top 5 Technical Pearls

Experts provide their top technical tips for cTACE, portal vein embolization, drug-eluting embolic TACE, radiation segmentectomy, parenchyma-sparing Y-90 with flow diversion, challenging ablations, ablation of poorly visualized hepatic tumors, and treatment of parasitized extrahepatic arteries.

With Thierry de Baere, MD; Nadine Abi-Jaoudeh, MD, FSIR, CCRP; Robert J. Lewandowski, MD; Edward Kim, MD, FSIR; Raul N. Uppot, MD; Amanda Smolock, MD, PhD; David S. Wang, MD, FSIR; and Daniel Sze, MD, PhD

CONVENTIONAL TRANSARTERIAL CHEMOEMBOLIZATION

THIERRY DE BAERE, MD

PEARL 1

Selectivity with a microcatheter positioned as close as possible to the tumor will maximize the antitumoral effect and minimize the collateral damage. The European Association for the Study of the Liver and European Society for Medical Oncology highlighted that transarterial chemoembolization (TACE) must be used in hepatocellular carcinoma (HCC) "selectively targetable" and "accessible to supraselective catheterization."[1]

PEARL 2

Angio cone-beam CT (CBCT) must be used to detect enhancing tumors and tumor feeders and guide tumor targeting to cover all tumor volume, ideally with safety margins and faint portal vein filling.

PEARL 3

A water-in-oil Lipiodol (Guerbet LLC) emulsion must be injected where Lipiodol has propensity to reach tumor arteries and thus carry the drug to the tumor.[2] A water-in-oil emulsion is best obtained by incrementally adding a small aliquot of drug in the all-Lipiodol volume using the pumping method through a three-way stopcock. Direction of the emulsion is assessable with the "drop test."

PEARL 4

Additional embolization is required after delivery of the drug-in-Lipiodol emulsion, and "lipiodolization" is not acceptable.

PEARL 5

Immediate posttreatment multidetector CT or CBCT is mandatory to check complete tumor coverage, which is evaluated by the marked attenuation of Lipiodol deposit.

PORTAL VEIN EMBOLIZATION

PEARL 1

Accurate knowledge of the anatomy, volumetry, and preplanned procedural approach based on liver volumetry is mandatory, because the portal vein is known to have several possible variations and access is

highly dependent on its anatomy. Always remember, beyond the classic right or right extended segment 4 portal vein embolization (PVE), PVE can help with more extended or atypical surgery.

PEARL 2

The portal vein must be accessed according to the anatomy and territories to be embolized, as well as the chosen technique of embolization. Both ipsilateral and contralateral must be part of your practice. One is not superior to the other; rather, they are complementary.

PEARL 3

N-butyl cyanoacrylate (NBCA) is superior to other embolic materials and must be used for embolization, as demonstrated in randomized controlled trials (RCTs) and meta-analyses.[3,4] NBCA diluted from 1 to 3 to 1 to 7 with Lipiodol must be injected using the sandwich technique from distal to proximal portal branches.

PEARL 4

Short, dedicated 4- or 5-F catheters are much more user-friendly compared with long catheters. Use of a microcatheter is not my standard but can be reassuring for less experienced physicians.

PEARL 5

When the segment must be resected, segment 4 embolization has been demonstrated to improve outcomes. However, proceed with caution when performing embolization of segment 4 to avoid any nontarget embolization that can then preclude surgery.

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DRUG-ELUTING EMBOLIC TACE

NADINE ABI-JAOUDEH, MD, FSIR, CCRP

PEARL 1

My first reaction to writing on this topic was one sentence. My number 1 and only amazing pearl is: Do not do drug-eluting embolic TACE (DEE-TACE); please do conventional TACE (cTACE) with a mixture of several drugs using the "touch the tumor" technique (also known as superselective) until you see portal vein opacification. Why? Because a meta-analysis of RCTs of HCC comparing cTACE with single versus combination drugs and DEE-TACE showed that multidrug cTACE had the best results. The best overall responses and outcomes with TACE are with a superselective approach and opacification of the portal venous system. Does that mean that DEE-TACE is over? Not at all. The technology stagnated and it needs improvements, but its potential and uses are real. Any technology or product that is stagnant can be considered obsolete and will be eliminated out of the treatment paradigm within a few years.

PEARL 2

If you are going to perform DEE-TACE for HCC and have access to idarubicin in lyophilized form, use idarubicin-loaded beads. Doxorubicin, which remains the most used agent for HCC, has no efficacy against HCC, as demonstrated by in vitro cell line studies, animal studies, and phase 3 RCTs. Epirubicin is a better alternative if you cannot get idarubicin.

PEARL 3

For colorectal liver metastasis, use irinotecan-loaded beads. Do not use DEE-TACE in neuroendocrine metastasis. They are associated with high biliary complications.

PEARL 4

Smaller beads are better because they have been shown to have more uniform and deeper penetration of the tumor vessels, allowing for more uniform and better distribution of the drug. They have a greater surface area and longer suspension. Beads that are 75 µm or smaller are preferable to larger beads.

PEARL 5

Selective technique is important. The ideal endpoint is maintained forward flow in the vessel without tumor blush. This was determined with the SACE (subjective angiographic chemoembolization endpoint) scale for embolization in retrospective trials, and although it was never validated in prospective trials, it is the best we have.

SUMMARY

There are certainly advancements being worked on in DEE-TACE. One example is improving the drugs that can be loaded on DEE to enable physicians to tailor the drug to the cancer being treated without current limitations that the drug must be hydrophilic and have an electrical charge. The type of DEE is also improving, with gel and foams being explored to enable an occlusion of smaller vessels more reliably to induce ischemia instead of hypoxia. Stay tuned for some exciting developments on the horizon!

RADIATION SEGMENTECTOMY

ROBERT J. LEWANDOWSKI, MD

Radiation segmentectomy is defined as the ablative segmental application of yttrium-90 (Y-90) microspheres for curative intent when targeting ≤ 2 hepatic segments. Its outcomes are manifested by high imaging complete response rates based on tumor necrosis (ie, mRECIST [modified Response Evaluation Criteria in Solid Tumors]), very low local recurrence rates, and high rates of explant complete pathologic necrosis. Optimization of radiation segmentectomy requires careful patient selection, expert angiographic technique using microcatheters and catheter-based CTA (eg, CBCT), and threshold dosimetry. Herein are five technical pearls to achieve best outcomes.

The best candidates for radiation segmentectomy have peripheral tumor(s) located in sparable hepatic angiosomes that are amenable to segmental transcatheter intra-arterial treatment. There is no definite percent liver treated threshold for Child-Pugh A patients, but Child-Pugh B patients do best when treating < 15% of the liver volume.

Tumor targeting should be confirmed with both digital subtraction angiography and CTA; the latter is critical in ensuring appropriate tumor targeting and confirming an adequate treatment margin. It is this ability to prospectively and consistently understand the treatment margin of radiation segmentectomy that provides an advantage of this therapy over thermal ablation in terms of local recurrence outcomes. Because of this, technical aspects of CTA are critical for best outcomes from radiation segmentectomy.

An example of best CTA practice is ensuring there is no reflux of angiographic contrast during image acquisition, which would mislead the interventional radiologist regarding both adequate tumor targeting and treatment margin.

Current practice for radiation segmentectomy, informed from radiology-pathology explant correlation studies, is based on threshold dosimetry with the intent of achieving a minimum radiation-absorbed dose to the tumor-bearing segment(s). This threshold dose assumes homogeneous microsphere deposition within the targeted treatment zone and does not require advanced dosimetry software.

The threshold radiation-absorbed dose for HCC has evolved from 190 Gray to 400 Gray, with more recent publications pushing this number even higher. Future work needs to study the maximum tolerated dose of radiation segmentectomy in HCC and other primary and secondary hepatic malignancies. Maximum tolerated dose, a guiding principle for colleagues in medical oncology and radiation oncology, needs to be embraced by the interventional radiology community.

PARENCHYMA-SPARING Y-90 WITH FLOW DIVERSION

EDWARD KIM, MD, FSIR

PEARL 1 Assess flow with CBCT at a rate of 0.5 mL/second.

PEARL 2 If flow does not preferentially go to the tumor, consider flow diversion.

PEARL 3 Use distal balloon occlusion or an embolic to drive flow into tumor versus normal parenchyma.

PEARL 4 If there is an arterioportal shunt, potentially access the portal and occlude the portal branch with the shunt with an occlusion balloon, repeat CBCT, and inject macroaggregated albumin (MAA).

PEARL 5 If there is a transjugular intrahepatic portosystemic shunt (TIPS) with a high lung shunt, consider balloon occlusion of the TIPS with repeat MAA study to reassess the lung shunt.

CHALLENGING ABLATIONS

RAUL N. UPPOT, MD

Image-guided ablation is an established pillar of interventional oncology. It is an accepted treatment option for oncologists seeking to manage solid organ tumors and for palliative care and pain specialists to help manage pain. Recent advances in ablation with introduction of new tools such as smaller-caliber radiofrequency (RF) probes, transurethral ablation probes, pulsed electrical field (PEF) ablation, and histotripsy have expanded the scope of ablation. With these advances in mind, the following are my top five technical pearls for challenging ablations.

PEARL 1 Most solid organ tumors can now be targeted and treated with ablation. Ablation should always be considered as a treatment option for almost any solid organ tumor in the body. With an increasing body of evidence for local tumor control in multiple organs, if a patient is not a surgical candidate and not responding to standard chemotherapy, ablation may be an option for local control or to debulk. Image-guided ablation has been used for local control of tumors in the kidneys, liver, lung, adrenals, pancreas and soft tissue, but it is now being applied for local control of tumors in the thyroid,[1] breast,[2] prostate,[3] and even the brain.[4,5]

PEARL 2 Treat large tumors with staged ablations or embolization plus ablation. Previously, ablations were limited to tumors ≤ 4 cm. Advances in ablation technology now allow for treatment of larger tumors for debulking. For large tumors ≥ 5 cm, two options for debulking include embolization first followed by ablation, or staged ablation with serial planned ablations to debulk portions of the tumor over several weeks.

PEARL 3 Know the strengths and limitations of each ablation device and select your equipment wisely. From a cost perspective, RF ablation is a good option for ablation. To efficiently destroy tumor using small caliber probes with large thermal volumes or when bleeding is a concern, microwave ablation is a good option. For visualizing ablation zones, treating larger tumors, and for ablation for pain control, cryoablation is a good option. If a tumor is close to a critical structure such as the bowel or gallbladder, irreversible electroporation and PEF ablation are good options but can only ablate a small volume of tissue.

PEARL 4 Be knowledgeable of adjunctive maneuvers to aid with image-guided ablations. If there is concern for potential ureteral injury, have a urologist place a ureteral stent and do pyeloperfusion.[6] To treat tumors close to bowels or other critical structures, perform hydro- or pneumodissection or even colon deflation to displace organs away from critical structures.[7] If treating a lung lesion, high liver dome, or upper

renal or adrenal lesion, consider high-frequency jet ventilation to help minimize diaphragmatic excursion and motion.[8]

PEARL 5

Be open minded when targeting lesions for ablation and be aggressive in ensuring adequate coverage. If lesions can easily be seen with ultrasound, use ultrasound to place a probe. Always be ready to use ultrasound or CT with contrast to visualize lesions for targeting. If ultrasound or contrast does not help visualize lesions, be open to using various image fusion software that can combine MRI with CT or ultrasound.[9]

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ABLATION OF POORLY VISUALIZED HEPATIC TUMORS

AMANDA SMOLOCK, MD, PHD

PEARL 1

Use general anesthesia for all cases. This allows for respiratory control and breathing maneuvers to help with visualization and accessibility, particularly for challenging locations such as high hepatic dome tumors.

PEARL 2

Tumors that are poorly visualized by ultrasound can be tagged with Lipiodol to improve visualization. Transarterial infusion of Lipiodol alone or cTACE can be performed to stain tumors. Lipiodol staining can improve both ultrasound and CT visualization to guide needle placement.

PEARL 3

Use contrast to improve tumor conspicuity. Contrast agents for both ultrasound and CT can be given to improve visualization for targeting. Note that contrast agents are dynamic and will not persist but can aid at critical points within the procedure for needle targeting.

PEARL 4

Use available software assistance programs. Several navigation, fusion imaging, and margin assessment software packages exist that can be used separately or together help ensure adequate targeting and complete treatments.

PEARL 5

MR-guided ablation can be performed for tumors not visible by ultrasound or CT. MR-compatible probes and equipment allow for the possibility of performing ablation in the MR environment for tumors best seen by MRI.

TREATMENT OF PARASITIZED EXTRAHEPATIC ARTERIES

DAVID S. WANG, MD, FSIR AND DANIEL SZE, MD, PHD

PEARL 1

Know the risk factors that predict the presence of parasitized extrahepatic collateral supply to intrahepatic tumors (eg, peripheral location, partially exophytic, prior transarterial therapy) and the spectrum of candidate supplying extrahepatic arteries based on tumor location (eg, right inferior phrenic artery for tumors in contact with the right hemidiaphragm or in the bare area of the liver, internal mammary artery for tumors in the anterior liver).[1,2]

PEARL 2

For preprocedural planning, a high-quality contrast-enhanced CT with arterial phase imaging and thin slices is highly

useful for identifying potential extrahepatic collateral arterial supply to hepatic tumors.

Intraprocedurally, hepatic C-arm CT arteriograms with contrast administered from a proximal catheter or microcatheter position (eg, common hepatic artery) is recommended so that a broader perfusion territory is evaluated. Accounting for variant hepatic arterial anatomy, a hepatic territory devoid of parenchymal or tumor enhancement should raise suspicion for parasitized supply from an extrahepatic collateral. In the absence of high-quality preprocedural arterial phase cross-sectional imaging, abdominal aortography with contrast administered from the level of T8 can be performed to assess for hypertrophy of a potential extrahepatic collateral artery. Any suspected extrahepatic collateral artery should be individually interrogated.

Gain experience with catheterization of the right inferior phrenic artery. The right inferior phrenic artery is the most common source of parasitized extrahepatic supply to liver tumors.

To prepare for radioembolization, superselective embolization of identified parasitized extrahepatic arteries with minor supply to intrahepatic tumors using medium- to large-size particles (minimum 300-500 µm) without or with coils to stasis can be performed to redistribute arterial supply to an intrahepatic artery, allowing for consolidation of Y-90 microsphere delivery sites.[2] Coil embolization alone can lead to subsequent recruitment of new extrahepatic collaterals. ■

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Portions of this article were presented at the annual Symposium on Clinical Interventional Oncology (CIO), held September 22-24, 2023. Visit www.theiomeeting.com for more information.

Thierry de Baere, MD
Gustave Roussy Cancer Centre, University Paris-Saclay
Villejuif, France
debaere@igr.fr

Nadine Abi-Jaoudeh, MD, FSIR, CCRP
University of California Irvine Health
Orange, California
nadine@hs.uci.edu

Robert J. Lewandowski, MD
Northwestern Medicine
Chicago, Illinois
r-lewandowski@northwestern.edu

Edward Kim, MD, FSIR
Mount Sinai Medical Center
New York, New York
edward.kim@mountsinai.org

Raul N. Uppot, MD
Massachusetts General Hospital
Boston, Massachusetts
uppot.raul@mgh.harvard.edu

Amanda Smolock, MD, PhD
Medical College of Wisconsin
Milwaukee, Wisconsin
asmolock@mcw.edu

David S. Wang, MD, FSIR
Stanford University
Stanford, California

Daniel Sze, MD, PhD
Stanford University
Stanford, California

Disclosures

Prof. de Baere: Consultant to AstraZeneca, Boston Scientific Corporation, Guerbet, Johnson & Johnson, Quantum Surgical, and Terumo; receives institutional grants/research support from Terumo, and Quantum Surgical; speakers bureau for Terumo, Guerbet, and Boston Scientific Corporation.
Dr. Abi-Jaoudeh: Principal Investigator on research grants and/or clinical trials at University of California that are sponsored or have received financial support from Philips Medical Systems Inc, Teclison Limited Inc, Guerbet SA, Varian Inc, Instylla HES Inc, BlackSwan Vascular Inc, Sirtex Medical Ltd, and AngioDynamics Inc; has served on advisory boards with Genentech F. Hoffmann-La Roche Ltd, QED Therapeutics Inc, Eisai, Lynx Group LLC, AstraZeneca Inc., and Pfizer.
Dr. Lewandowski: Consultant to Boston Scientific Corporation and ABK.
Dr. Kim: Advisory board for Boston Scientific Corporation.
Dr. Uppot: Consultant to Boston Scientific Corporation and the German Accelerator.
Dr. Smolock: Advisor and shareholder, HistoSonics, Inc.; consultant, speaking faculty, and grant recipient to NeuWave Medical; consultant to Varian; advisor board and CME Project Steering Committee member for AstraZeneca.
Dr. Wang: None.
Dr. Sze: Data and safety monitoring board for W.L. Gore, Replimune, and FluidX; Editor-in-Chief of JVIR.