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Image Guided Procedures and Response Assessment It is Time to Move from Anatomic to Physiologic Imaging

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Minimally invasive image guided procedures are commonplace in nearly all areas of medicine. This is particularly true for the management of malignancies where initial diagnosis usually involves image-guided biopsy and treatment may involve image guided locoregional therapy such as tumor ablation or Transarterial Chemoembolization (TACE) [1-3]. Currently, the intra-procedural guidance and subsequent follow up for most of these procedures is based on gross anatomic visualization with CT, MRI, Ultrasound, and Fluoroscopy. The most important endpoint in cancer treatment is overall survival. Nonetheless, tumor response and time to progression are commonly used, imaging based, surrogate endpoints for assessment of efficacy. Ideally image based guidance and assessment of treatment response would evaluate the early mechanism of action of therapeutic and not only downstream resulting tumor shrinkage. Usual contrast enhanced imaging provides relatively general semi-quantitative assessment of perfusion and perhaps tissue viability. However, except for invasive angiography, it is currently not practical to perform real time enhanced or physiologic imaging during a procedure. A number of emerging functional, physiologic and molecular imaging approaches offer the promise of improved intra-procedural guidance and meaningful assessment of the actual mechanism of action of locoregional and targeted therapies. Furthermore, novel fusion/navigation approaches allow real time fusion of functional/physiological imaging with ultrasound or fluoroscopy for intra-procedural guidance [4]. These approaches may optimize tumor specific image guided interventions and help advance proteomics, targeted therapy and personalized medicine, were tumor cell protein expression is targeted or used to guide treatment [5]. Furthermore, they may better guide biopsies, increasing yield and reducing sample error. This has been a focus of a number of NIH/NCI initiatives including the Cancer Imaging Program (CIP) and Image Response Assessment Team (IRAT).

Emerging enhanced dynamic physiologic imaging, such as Dynamic Contrast Enhanced (DCE) CT/MRI or Contrast Enhanced Ultrasound, is beginning to be incorporated into clinical care. DCE-MRI or CT allows determination of tissue blood flow, blood volume, vascular permeability and mean transit times through the intra- and extravascular spaces [6,7]. Diffusion Weighted MRI (DWI) provides imaging of free unrestricted water associated with tissue edema, fibrosis, necrosis and apoptosis allowing evaluation of tumor viability at the cellular level [8,9]. Blood oxygen level-dependent (BOLD) magnetic resonance imaging (MRI) has been utilized as a sensitive and non-invasive tool to monitor the oxygenation state and blood perfusion of tissue [10]. A number of radio nuclides allow physiologic and molecular imaging. (18)F Flourodeoxy Glucose positron emission tomography (FDG-PET) is part of standard imaging evaluation for a large number of neoplasms since metabolically active tumor cells have increased glucose uptake [11]. Thymidine analog 3'-deoxy-3'-18F-fluorothymidine (18F-FLT), is a new radiopharmaceutical for clinical PET that specifically visualizes proliferating tissue which permits estimation of tumor thymidine kinase-1 expression, and thus, cell proliferation [12]. Emerging PET imaging of hypoxia, with agents such as 18F Fluoromisonidazole (FMISO), has great potential for assessing tumor response, when the mechanism of action is reduction of blood flow/ischemia as with anti-angiogenic therapies and TACE [13]. These modalities can also be applied to image guided biopsies and percutaneous tumor ablation, to guide needle placement into viable tumor tissue, which at times may not be conspicuous, particularly with non-enhanced imaging [14]. However, it is not currently practical to perform procedures under PET guidance or during actual contrast enhancement with CT or MRI.

Emerging technologies allow fusion of images from PET or DCE MRI/CT with real time ultrasound to guide the biopsy needle or treatment to viable FDG avid or enhancing tumor [15]. Recently emerging cone beam CT angiography systems also allow real time multi-planar fusion of angiography with any DICOM (Digital Imaging and Communications in Medicine) imaging data, for guidance during fluoroscopic/angiographic procedures such as biopsies, TACE and Tumor Ablation [16]. Ultrasound contrast agents, consisting of a gas core encapsulated by a shell of lipid monolayer or cross-linked albumin [17], may also be used for real time guidance depicting tumor vascularity sensitively and accurately [18,19,20]. To date, no Ultrasound contrast agents have received approval from the FDA for radiological applications in the USA and only two are approved for cardiac left ventricular opacification. Kono et al. demonstrated residual tumor blood flow on CEUS performed at 2 or more days after transarterial chemoembolization may be predictive of tumor outcome that currently requires 3 months to be reliably detected by computed tomography and/or magnetic resonance imaging [21].

Transarterial Chemoembolization (TACE) is used for a number of intrahepatic primary and metastatic malignancies and has been shown to improve survival in patients with Hepatocelular Carcinoma [22,23]. TACE efficacy is attributable to direct embolization of the tumor vasculature and infusion of high dose localized chemotherapy resulting in ischemic as well as cytotoxic injury. The sequence of tumor response involves devascularization, microenvironmental changes and tumor necrosis with later resultant reduction in tumor diameter. The reduction in overall tumor size may take at least a month to be seen on anatomic imaging, while devascularization and reduced perfusion, occurs immediately. Conventional anatomic imaging endpoints including Response Criteria in Solid Tumors (RECIST) [24] and World

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Health Organization (WHO) Criteria [25], in which single long axis or bi-dimensional linear measurements are made across the tumor, are likely not adequate for assessment following locoregional therapy [26,27]. The delivery of the therapeutic, subsequent intratumoral distribution and ultimate efficacy is directly related to tumor perfusion, vascular permeability, and interstitial transit. Therefore, assessment of tumor physiology, using these advances in imaging, can help to guage and optimize the procedure in real time.

When evaluating molecular targeted and locoregional therapy, recent imaging based response criteria has focused on measurements of viable enhancing tumor and non-enhancing tumor necrosis on CT or MRI as described in The European Association for the Study of the Liver (EASL) criteria and the Modified RECIST Assessment (mRECIST) [28]. However, evolving techniques in Dynamic Contrast Enhanced (DCE) MRI/CT and DWI MRI allow the determination of microvascular parameters such as perfusion and permeability and apoptosis, which may provide early physiologic assessment following locoregional therapy [8,9]. Furthermore, Whal et al. proposed a PET based Response Criteria in Solid Tumors (PERCIST) [29]. Metabolic volume and total lesion glycolysis, according to PERCIST, predicted survival better than RECIST following Yitrium 90 radioembolization locoregional therapy of colorectal metastases [30] as well as HCC response following TACE [31].

Emerging physiologic imaging approaches should be utilized to optimize intraprocedural guidance and response assessment of targeted and locoregional therapies.

References

1. Lewandowski RJ, Geschwind JF, Liapi E, Salem R (2011) Transcatheter intraarterial therapies: rationale and overview. Radiology 259: 641-657.
2. Smith KA, Kim HS (2011) Interventional radiology and image-guided medicine: interventional oncology. Semin Oncol 38: 151-162.
3. Ahmed M, Brace CL, Lee FT Jr, Goldberg SN (2011) Principles of and advances in percutaneous ablation. Radiology 258: 351-369.
4. Giesel FL, Mehndiratta A, Locklin J, McAuliffe MJ, White S, et al. (2009) Image fusion using CT, MRI and PET for treatment planning, navigation and follow up in percutaneous RFA. Exp Oncol 31: 106-114.
5. Silvestri A, Pin E, Huijbers A, Pellicani R, Parasido EM, et al. (2013) Individualized therapy for metastatic colorectal cancer. J Intern Med 274: 1-24.
6. Sourbron SP, Buckley DL (2013) Classic models for dynamic contrast-enhanced MRI. NMR Biomed 26: 1004-1027.
7. Ewing JR, Bagher-Ebadian H (2013) Model selection in measures of vascular parameters using dynamic contrast-enhanced MRI: experimental and clinical applications. NMR Biomed 26: 1028-1041.
8. Kamel IR, Bluemke DA, Ramsey D, Abusedera M, Torbenson M, et al. (2003) Role of diffusion-weighted imaging in estimating tumor necrosis after chemoembolization of hepatocellular carcinoma. AJR Am J Roentgenol 181: 708-710.
9. Kamel IR, Bluemke DA, Eng J, Liapi E, Messersmith W, et al. (2006) The role of functional MR imaging in the assessment of tumor response after chemoembolization in patients with hepatocellular carcinoma. J Vasc Interv Radiol 17: 505-512.
10. Choi JW, Kim H, Kim HC, Lee Y, Kwon J, et al. (2013) Blood oxygen level-dependent MRI for evaluation of early response of liver tumors to chemoembolization: an animal study. Anticancer Res 33: 1887-1892.
11. Sharma B, Martin A, Zerizer I (2013) Positron emission tomography-computed tomography in liver imaging. Semin Ultrasound CT MR 34: 66-80.
12. Eckel F, Herrmann K, Schmidt S, Hillerer C, Wieder HA, et al. (2009) Imaging of proliferation in hepatocellular carcinoma with the in vivo marker 18F-fluorothymidine. J Nucl Med 50: 1441-1447.
13. Hoigebazar L, Jeong JM (2013) Hypoxia imaging agents labeled with positron emitters. Recent Results Cancer Res 194: 285-299.
14. Venkatesan AM, Kadoury S, Abi-Jaoudeh N, Levy EB, Maass-Moreno R, et al. (2011) Real-time FDG PET guidance during biopsies and radiofrequency ablation using multimodality fusion with electromagnetic navigation. Radiology 260: 848-856.
15. Abi-Jaoudeh N, Kruecker J, Kadoury S, Kobeiter H, Venkatesan AM, et al. (2012) Multimodality image fusion-guided procedures: technique, accuracy, and applications. Cardiovasc Intervent Radiol 35: 986-998.
16. Abi-Jaoudeh N, Mielekamp P, Noordhoek N, Venkatesan AM, Millo C, et al. (2012) Cone-beam computed tomography fusion and navigation for real-time positron emission tomography-guided biopsies and ablations: a feasibility study. J Vasc Interv Radiol 23: 737-743.
17. Alzaraa A, Gravante G, Chung WY, Al-Leswas D, Morgan B, et al. (2013) Contrast-enhanced ultrasound in the preoperative, intraoperative and postoperative assessment of liver lesions. Hepatol Res 43: 809-819.
18. Kim HJ, Kim TK, Kim PN, Kim AY, Ko EY, et al. (2006) Assessment of the therapeutic response of hepatocellular carcinoma treated with transcatheter arterial chemoembolization: comparison of contrast-enhanced sonography and 3-phase computed tomography. J Ultrasound Med 25: 477-486.
19. Takizawa K, Numata K, Morimoto M, Kondo M, Nozaki A, et al. (2013) Use of contrast-enhanced ultrasonography with a perflubutane-based contrast agent performed one day after transarterial chemoembolization for the early assessment of residual viable hepatocellular carcinoma. Eur J Radiol 82: 1471-1480.
20. Numata K, Tanaka K, Kiba T, Saito S, Isozaki T, et al. (2001) Using contrast-enhanced sonography to assess the effectiveness of transcatheter arterial embolization for hepatocellular carcinoma. AJR Am J Roentgenol 176: 1199-1205.
21. Kono Y, Lucidarme O, Choi SH, Rose SC, Hassanein TI, et al. (2007) Contrast-enhanced ultrasound as a predictor of treatment efficacy within 2 weeks after transarterial chemoembolization of hepatocellular carcinoma. J Vasc Interv Radiol 18: 57-65.
22. Lo CM, Ngan H, Tso WK, Liu CL, Lam CM, et al. (2002) Randomized controlled trial of transarterial lipiodol chemoembolization for unresectable hepatocellular carcinoma. Hepatology 35: 1164-1171.
23. Llovet JM, Real MI, Montaña X, Planas R, Coll S, et al. (2002) Barcelona Liver Cancer Group. Arterial embolisation or chemoembolisation versus symptomatic treatment in patients with unresectable hepatocellular carcinoma: a randomised controlled trial. Lancet 359: 1734-1739.
24. Therasse P, Arbuck SG, Eisenhauer EA, Wanders J, Kaplan RS, et al. (2000) New guidelines to evaluate the response to treatment in solid tumors. European Organization for Research and Treatment of Cancer, National Cancer Institute of the United States, National Cancer Institute of Canada. J Natl Cancer Inst 92: 205-216.
25. Miller AB, Hoogstraten B, Staquet M, Winkler A (1981) Reporting results of cancer treatment. Cancer 47: 207-214.
26. Forner A, Ayuso C, Varela M, Rimola J, Hessheimer AJ, et al. (2009) Evaluation of tumor response after locoregional therapies in hepatocellular carcinoma: are response evaluation criteria in solid tumors reliable? Cancer 115: 616-623.
27. Kudo M, Kubo S, Takayasu K, Sakamoto M, Tanaka M, et al. (2010) Response Evaluation Criteria in Cancer of the Liver (RECICL) proposed by the Liver Cancer Study Group of Japan (2009 Revised Version). Hepatol Res 40: 686-692.
28. Lencioni R, Llovet JM (2010) Modified RECIST (mRECIST) assessment for hepatocellular carcinoma. Semin Liver Dis 30: 52-60.
29. Wahl RL, Jacene H, Kasamon Y, Lodge MA (2009) From RECIST to PERCIST: Evolving Considerations for PET response criteria in solid tumors. J Nucl Med 50 Suppl 1: 122S-50S.
30. Fendler WP, Philippe Tiega DB, Ilhan H, Paprottka PM, Heinemann V, et al. (2013) Validation of several SUV-based parameters derived from 18F-FDG PET for prediction of survival after SIRT of hepatic metastases from colorectal cancer. J Nucl Med 54: 1202-1208.
31. Song MJ, Bae SH, Yoo IeR, Park CH, Jang JW, et al. (2012) Predictive value of Â¹â¸F-fluorodeoxyglucose PET/CT for transarterial chemolipiodolization of hepatocellular carcinoma. World J Gastroenterol 18: 3215-3222.