



CT Perfusion Imaging and Oncology

- CT perfusion (CTp) imaging specifically evaluates blood flow, blood volume, mean transit time, and vascular permeability from dynamic changes in contrast enhancement
- Although CTp has been used for stroke evaluation, it has an emerging role in the evaluation of tumor angiogenesis
- CTp has potential for routine application in oncologic imaging for diagnosis, risk stratification, and therapeutic monitoring

Contrast enhanced CT imaging has long been the standard of care for the diagnosis and staging of cancers in the abdomen (Figure 1), due to the differences in contrast enhancement of tumor tissue versus normal background tissue. Perfusion CT (CTp) offers the potential of more detailed evaluation of tumor vasculature. Visualization of tumors can be attributed to abnormalities in the vasculature. Angiogenesis is an important step in the process of cancer development and is essential for tumor growth. Angiogenic vasculature in tumors generally has a high microvasculature density with vessels that are dilated, tortuous, have abnormal branching patterns, and lack the well-organized structure of arterioles, capillaries, and veins found in normal tissues. As a result, blood volume and blood flow are abnormally high in tumor tissue. In addition, tumor blood vessels are immature and leaky. Therefore, contrast agents pass through the tumor vascular epithelium into the extravascular space more rapidly than in the normal tissue. As a result, the attenuation due to contrast agents is greater in the tumor than the surrounding tissue.

Microvessel density has been established as a prognostic indicator for many cancers and the initiation of angiogenesis is thought to be a requirement for metastasis. The importance of angiogenesis to the progression of cancer has sparked interest in the development of several new drugs that target the process of angiogenesis, such as bevacizumab (Avastin) and sorafenib. These drugs do not exhibit the same cytotoxicity as standard chemotherapeutic drugs and do not necessarily reduce the size of tumors, which is the standard method for assessing tumor response. Measuring changes in the vasculature itself would be more appropriate, which can be accomplished with a number of radiologic techniques, including CT.

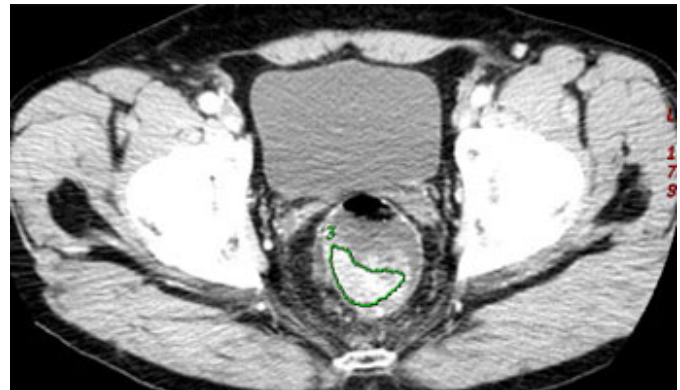


Figure 1. Axial contrast enhanced CT image of the pelvis shows rectal cancer as an irregular enhancing mass in the rectum causing wall thickening (outlined in green).

Perfusion CT

The concept of perfusion CT (CTp) has existed for many years, but has only recently emerged as a practical method of scanning since the development of high speed multidetector CT (MDCT) and commercially available software for data analysis. Perfusion CT now has an established clinical role in stroke management and shows promise in oncology for diagnosis, risk stratification, and therapeutic response monitoring.

CTp is performed with the acquisition of a series of images before, during, and after the passage of a bolus of contrast through the vasculature. During image acquisition, the CT table does not move and the scan is limited by the width of the detectors, which is 2 cm in 4-16 slice scanners and 4 cm in 64-slice scanners. The selection of the region of interest is therefore critical. Breath-holding is essential for perfusion CT of the

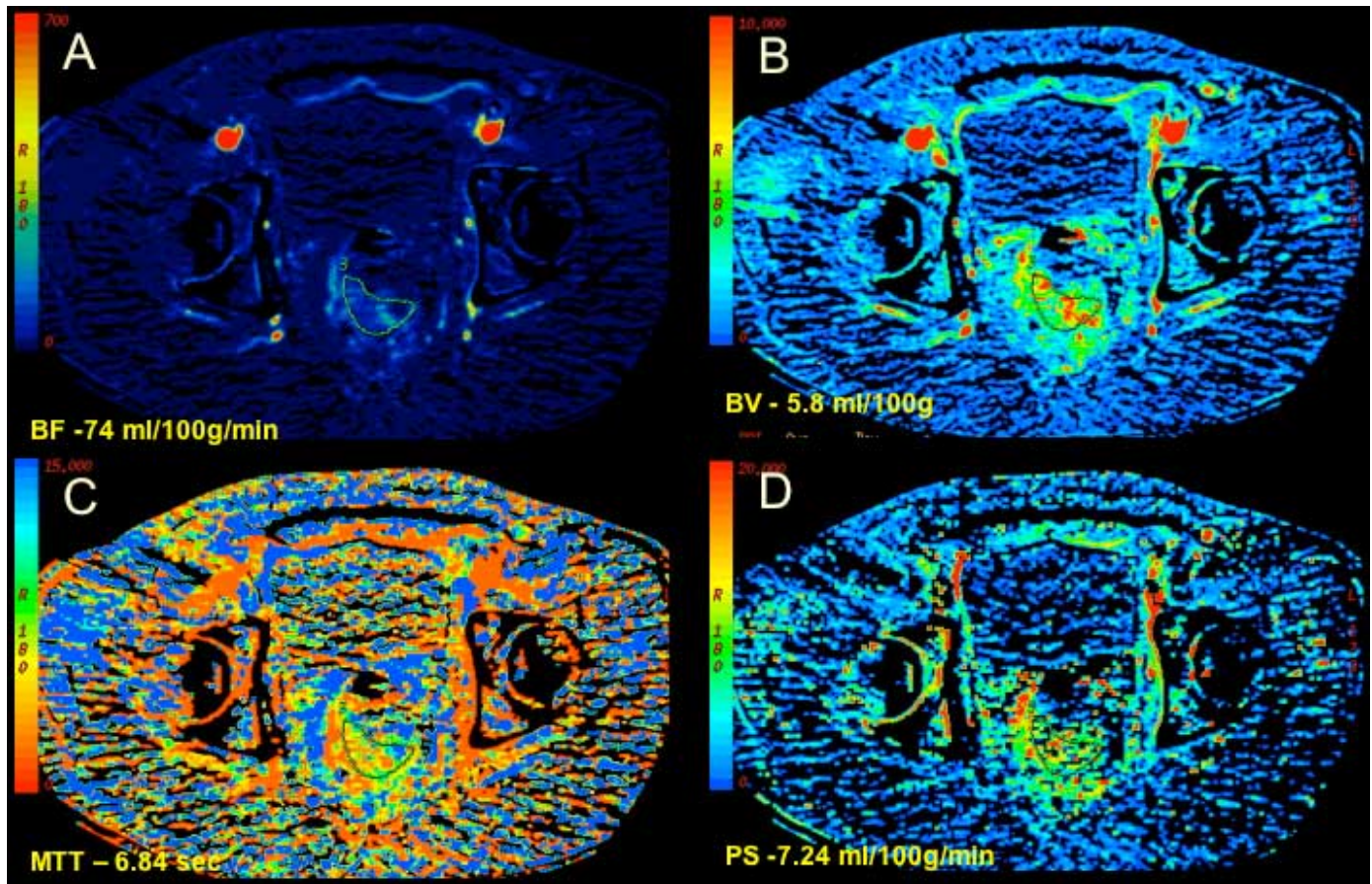


Figure 2. Perfusion CT (CTp) scans of the tumor shown in Figure 1. (A) Blood flow (mean, 74 ml/100 g/min); (B) Blood volume (mean, 5.8 ml/100 g); (C) mean transit time (MTT) (6.84 seconds); and (D) permeability-surface area product (mean, 7.24 ml/100 g/min).

upper viscera in order to avoid motion artifacts. When examining tumors in close proximity to hollow viscera, it is necessary to distend the hollow viscus with saline or water for optimal evaluation.

In the typical CTp protocol, dynamic phase images are acquired at the rate of one per second for a period of 40-60 seconds after the injection of 40-50 ml of contrast at a rate of 4-7 ml/sec. This dynamic phase is followed by a second phase in which images are acquired at the rate of one every 10 seconds for 2 minutes. The dynamic data is used to calculate blood volume and flow, while the second phase provides data on vascular permeability.

Data Analysis

The chronological changes in x-ray attenuation during CTp are directly proportional to the concentration of iodinated contrast material in the tissues. During the first pass of the contrast agent (dynamic phase), the agent is largely confined to within the vasculature and the change in attenuation largely depends on blood flow and blood volume. In the later phase, differences in concentration of the agent in the extravascular space are detected, which are dependent on permeability of the vasculature.

Perfusion parameters are calculated through mathematical modeling, using commercially available software. In the deconvolution method, the mean transit time (MTT) and estimated values for blood flow and blood volume are calculated from the dynamic phase, and the permeability surface-area product (PS) is calculated from the delayed washout of the contrast material (Figures 2).

Oncologic Applications

A number of studies in a variety of cancers have provided clinical evidence for the value of CTp for tumor imaging for lesion characterization (differentiating between benign and malignant), depiction of occult malignancy, staging of cancers and providing prognostic information, and monitoring the therapeutic effects of both antiangiogenic (Figure 3) and other treatment regimes.

For example, in head and neck cancer, evidence is emerging that malignant lesions have a significantly lower MTT than benign lesions and that tumors with a low perfusion rate are less likely to respond to radiotherapy, independent of tumor size. In the liver, CTp has been shown to increase the sensitivity of detecting hepatocellular carcinoma (HCC). In a study of

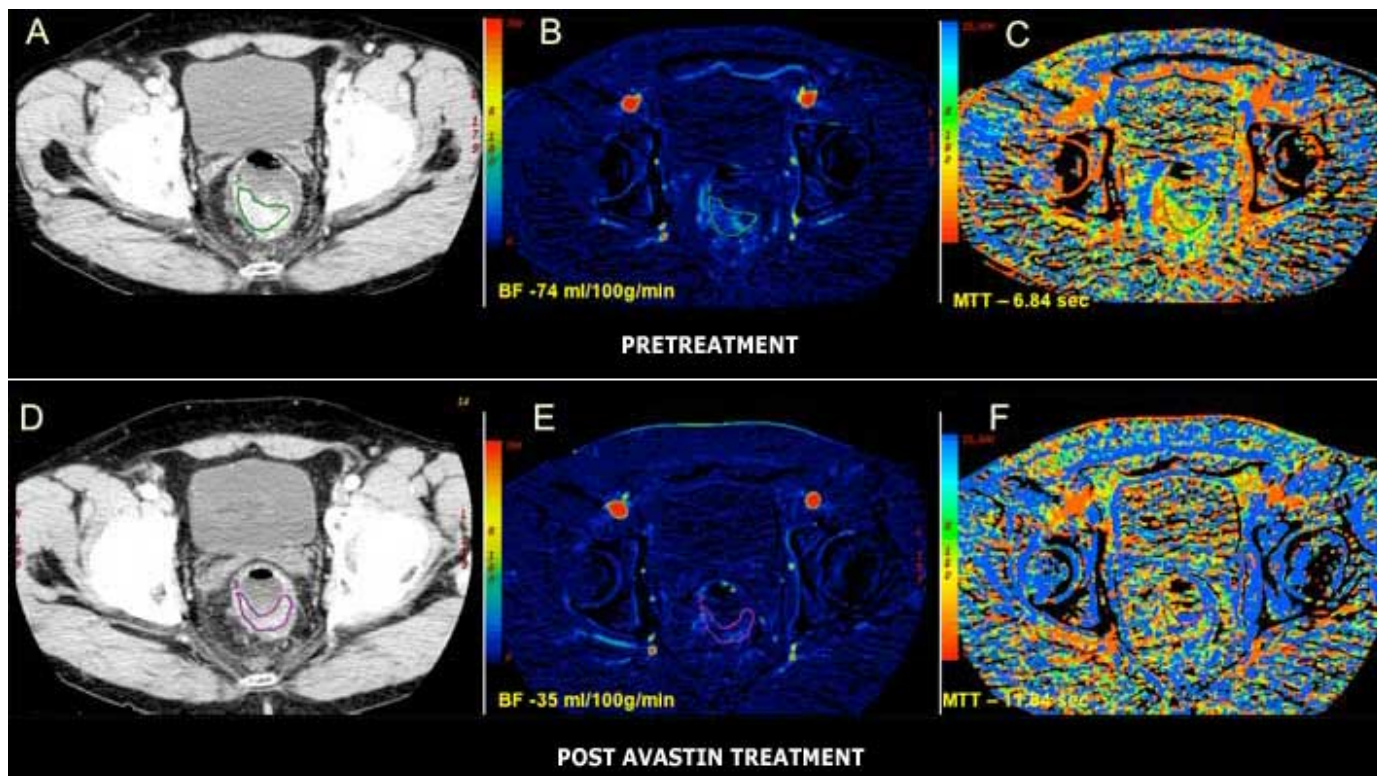


Figure 3. CTP images obtained before and after treatment with anti-angiogenic agent Avastin in a 64 year-old male with rectal cancer. (A) Pre-treatment axial contrast enhanced CT image in the dynamic phase shows the enhancing rectal carcinoma with corresponding colored perfusion maps demonstrating (B) elevated blood flow (74 ml/100 g/min) and (C) reduced MTT (6.84 sec). (D) Post treatment with Avastin axial contrast enhanced CT image shows reduced enhancement with corresponding colored perfusion maps demonstrating (E) reduction in blood flow (35ml/100g/min) and (F) increase in the MTT (11.8 sec).

the efficacy of the antiangiogenic drug, bevacizumab, on advanced HCC, changes in mean blood flow, blood volume, and mean PS in the tumors all significantly decreased within 10 days of initiation of treatment, while mean MTT significantly increased. It was also noted that patients with progressive disease have a lower mean MTT at baseline than those with partial response or stable disease. In rectal cancer patients who underwent radiation and chemotherapy prior to surgery, non-responders had lower baseline values of MTT and higher blood flow than responders. After the completion of radiation treatment and chemotherapy (6-8 weeks), there was a significant drop in blood flow and PS and an increase in MTT.

Scheduling

CT perfusion imaging is a research protocol at this time, not a routine practice. In order to schedule patients for this protocol, please contact [Dushyant Sahani, M.D.](#), at 617-726-3937.

Further Information

For further questions, please contact [Dushyant Sahani, M.D.](#), Director of CT Imaging Services, Abdominal Imaging and Intervention, Department of Radiology, Massachusetts General Hospital at 617-726-3937.

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References

- Folkman, J. (2002) *Role of angiogenesis in tumor growth and metastasis*. *Semin Oncol* **29**: 15-8
- Hermans, R, Meijerink, M, Van den Bogaert, W, Rijnders, A, Weltens, C and Lambin, P. (2003) *Tumor perfusion rate determined noninvasively by dynamic computed tomography predicts outcome in head-and-neck cancer after radiotherapy*. *Int J Radiat Oncol Biol Phys* **57**: 1351-6
- Meijerink, MR, van Waesberghe, JH, van der Weide, L, van den Tol, P, Meijer, S and van Kuijk, C. (2008) *Total-liver-volume perfusion CT using 3-D image fusion to improve detection and characterization of liver metastases*. *Eur Radiol*
- Miles, KA and Griffiths, MR. (2003) *Perfusion CT: a worthwhile enhancement?* *Br J Radiol* **76**: 220-231
- Sahani, DV, Kalva, SP, Hamberg, LM, Hahn, PF, Willett, CG, Saini, S, Mueller, PR and Lee, TY. (2005) *Assessing tumor perfusion and treatment response in rectal cancer with multisection CT: initial observations*. *Radiology* **234**: 785-92
- Zhu, AX, Holalkere, NS, Muzikansky, A, Horgan, K and Sahani, DV. (2008) *Early antiangiogenic activity of bevacizumab evaluated by computed tomography perfusion scan in patients with advanced hepatocellular carcinoma*. *Oncologist* **13**: 120-5

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