Extra window in oncology with vascular permeability analysis

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MR Permeability on the IntelliSpace Portal

With MR Permeability on the IntelliSpace Portal, it is possible to measure the leakage of gadolinium chelates into the extra-vascular extracellular space (EES). The most important use relates to oncology of the prostate, breast and brain.

Vascular Permeability

One characteristic of cancer development is that fast cell growth needs to be supported by extra blood and nutrient supply. This is often characterized by growth of extra blood vessels from existing vessels, called angiogenesis. While angiogenesis is a normal process, e.g. in wound healing, it is also a fundamental step in the transition of tumors towards a malignant state.

Normal values for permeability are organ specific. Permeability in the brain is unique in that it has a blood brain barrier (BBB), which effectively separates circulating blood from the brain extracellular fluid in the central nervous system for a healthy human being. The cells in the vessel wall will restrict diffusion of the larger objects like bacteria and certain molecules into the brain, but allow small molecules like O_2, hormones and CO_2 into the tissue. Therefore, the measured permeability in the healthy brain is close to zero.

The vessels in the prostate, however, are much more permeable, with values larger than zero for both normal and cancerous tissue. In the case of brain imaging, permeability analysis is potentially an important addition to anatomical imaging during the therapy follow-up of patients with brain tumors.

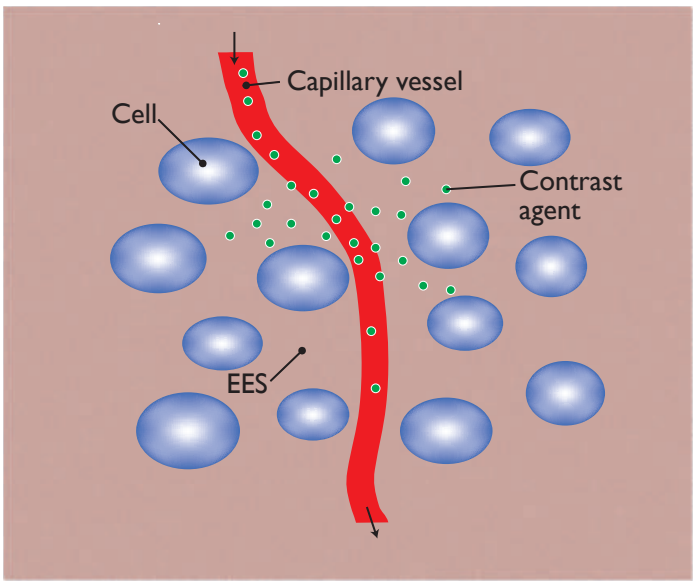

Fig.1. Schematic representation of physiology related to flow and permeability in blood vessels. Depending on the tissue characteristics, some of the contrast agent leaks into the space in between cells, the Extravascular Extracellular Space (EES). The contrast agent does not enter the cells, but will wash in and out of the EES.

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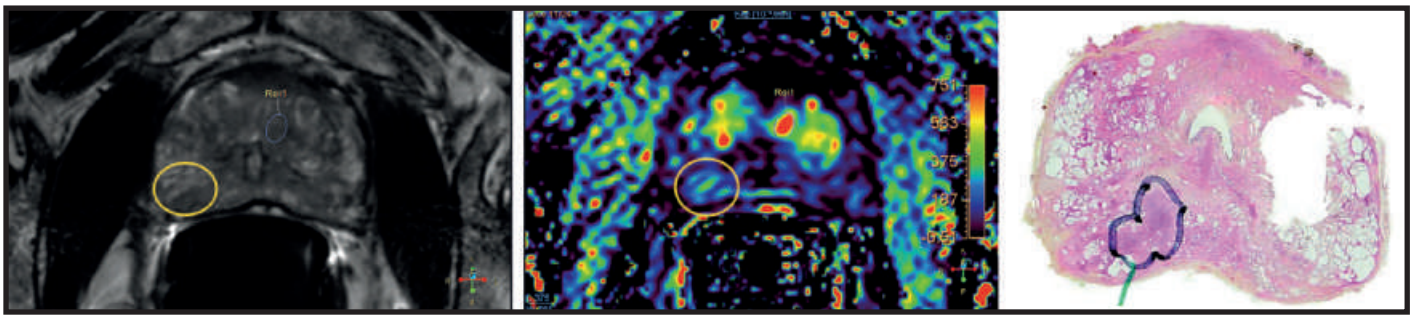
Fig. 2 Prostate evaluation: comparison of imaging and histology. From left to right, a T2w image, K_{ep} and a histology sample of the same region are shown. The hyperperfusion in the central part of the prostate indicates benign prostatic hyperplasia and is normal. The tumor focus shown by DCE, which was not clearly detected by the T2w image, is in the right peripheral zone, highlighted by a large yellow ellipse in the first two images, and a dark 'circle' marker on the histology sample on the right. Courtesy: Hôpital Edouard Herriot, Lyon, France.



Brain tumors, e.g. glioblastoma multiforme (GBM, e.g. Fig. 3), can be very aggressive and differentiation of therapy related tissue changes and tumor relapse is often challenging. There is emerging evidence that accurate monitoring of the tumoral vascular behavior may help in the distinction between these two entities. Dr. van Cauter further emphasizes that this technique, in which the acquisition sequence is T1-weighted, does not suffer from susceptibility artifacts as experienced with EPI-based sequences like T2* Perfusion and which make proper diagnosis of e.g. the frontobasal region very challenging. This can be of considerable importance, especially in post-surgery patients where the absence of distortions due to suture material and/or blood deposits enables a cleaner read and analysis of the images.

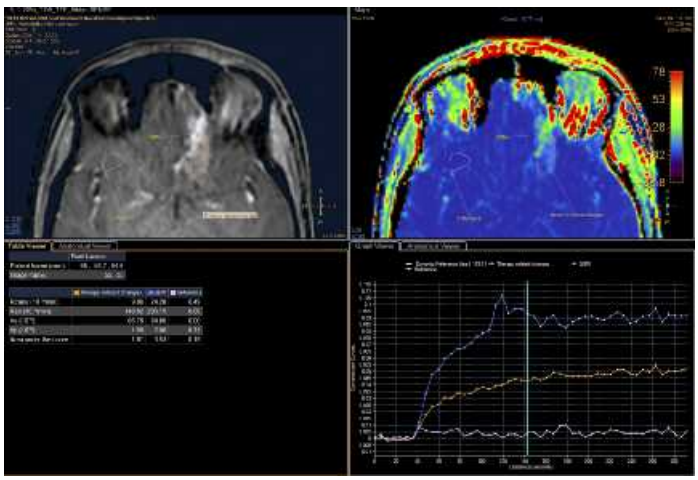


Fig. 3. An 18-year old female previously underwent surgical resection in the frontobasal region and combined radio/chemotherapy for a GBM. Also, the MRI three months post-radiotherapy showed contrast enhancement, initially suspected for tumor progression. However, DCE-perfusion (data above) was able to show regions indicating lower forms of leakage (orange region of interest and curve), indicative of therapy related changes like radio-necrosis. The control MRI six weeks later confirmed this: no tumor progression but a further diminished enhancement in these regions.
Courtesy: Katholieke Universiteit Leuven, Leuven, Belgium

Acquisition and Processing

The acquisition consists of 2 phases. Firstly, two separate 3D T1 acquisitions are made, with different flip-angles, which are used to determine the T1 relaxation time of the tissue. Following that, a Dynamic Contrast Enhanced (DCE) acquisition is performed. This is a high spatial and high temporal resolution dynamic T1 acquisition acquired while a bolus of contrast is injected [1].

At the Netherlands Cancer Institute (NKI-AVL) between 400 and 450 patients undergo such an exam for detection, localization and staging of prostate cancer annually. About 250 patients are subsequently treated with radiotherapy. Dr. van der Heide mentions that a quantitative analysis of the DCE measurements is particularly relevant for precise delineation of tumors for treatment with radiotherapy. This is even more important in cases of salvage radiotherapy, such as salvage brachytherapy.

On the IntelliSpace Portal, the Permeability analysis tool will combine the 3D T1 references and DCE aseries autoimatically and directly provide permeability results. One important element in the calculation is the Arterial Input Function (AIF) to fit all results to the Tofts model [1]. The MR Permeability package provides two ways to define the AIF. One is AIF modeling based on the provided injection protocol: the injection protocol must be defined by the user in the task guided user interface. Alternatively, the AIF can be identified by the user from the actual DCE data by the user, e.g. in the femoral artery in the case of prostate acquisitions.

The MR Permeability tool does not simply calculate maps. Instead it visualizes the combination of quantitative results with the source as well as relevant anatomical data: typically T2w images and diffusion related data, always geometrically aligned with the original DCE acquisition.

Permeability Parameters

The MR Permeability tool is based on the Tofts model [1] and the resulting parametric maps like K^{trans} and K_{ep} provide an image of the tracer kinetics behavior.

- The transfer constant K^{trans} describes the transfer of the diffusible tracer into the EES. This transfer will depend largely on the permeability, plus the flow of blood plasma that carries the contrast agent.
- The rate constant K_{ep} describes the clearance of the same tracer from the EES back to the blood plasma. Also here the permeability will influence the (efflux) rate. However, the efflux is further influenced by the volume of the EES compared to that of the blood plasma: if a tissue has a small percentage of EES there will be a large surface area product to enable the efflux rate.

According to Dr. van Cauter, the future of oncology work-ups will most likely be based on the combination of anatomical and a variety of functional imaging techniques like MR perfusion, diffusion and spectroscopy. Values like K^{trans} and K_{ep} by themselves do not provide an absolute truth, but they will improve monitoring of therapy effectiveness, especially when used in a multimodal approach.

Dr. Rouvière states that prostate cancer is hard to image. The key need is to guide prostate biopsy and provide useful information for patient management. In order to do so, one must provide position, volume and aggressiveness of cancer foci within the gland. With multi-parametric MRI (mp-MRI) the combination of T2w, DWI, and DCE imaging has yielded promising results in prostate cancer detection and localization [2, 3], but interpretation remains difficult. Although qualitative visual analysis of native DCE images is possible [4], quantitative data on perfusion could improve mp-MRI reproducibility, but adoption is hampered by unknowns about the quantification methods and the lack of easily available software. The MR Permeability analysis from Philips is an easy tool for quantification of permeability and will allow independent groups to characterize prostate cancer foci, and, hopefully, improve prostate cancer diagnostic and management.

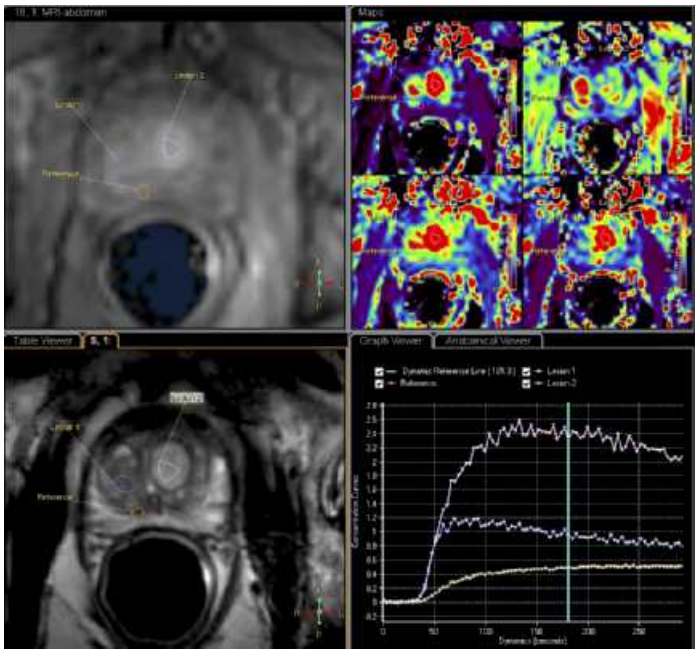


Fig. 4. This case displays hotspots in both the K^{trans} versus K_{ep} maps (color maps upper left and upper right) within the prostate. The spatial pattern in K^{trans} and K_{ep} is slightly different. The difference in the contrast uptake behavior is also recognized by the time intensity displays of lesion 1 and 2 located in two different areas.
Courtesy: The Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital (NKI-AVL).

References

1. P.S. Tofts et al. Estimating Kinetic Parameters from dynamic contrast-enhanced T1-weighted MRI of a diffusible tracer: standardized quantities and symbols. JMRI 10: 223-232 (1999).
2. Sciarra, A. et al. Advances in magnetic resonance imaging: how they are changing the management of prostate cancer. Eur Urol 59, 962-77 (2011).
3. Barentsz, J.O. et al. ESUR prostate MR guidelines 2012. Eur Radiol 22, 746-57 (2012).
4. Girouin, N. et al. Prostate dynamic contrast-enhanced MRI with simple visual diagnostic criteria: is it reasonable? Eur Radiol 17, 1498-509 (2007).

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