

# Brain Perfusion; How & Why

Nader Binesh, Ph.D.<sup>1</sup>; Marcel M. Maya, M.D.<sup>1</sup>; Helmuth Schultze-Haakh, Ph.D.<sup>2</sup>; Franklin G. Moser, M.D.<sup>1</sup>

<sup>1</sup>Department of Imaging, Cedars Sinai Medical Center, Los Angeles, CA, USA

<sup>2</sup>Siemens Medical Solutions, Cypress, CA, USA

## Introduction

Cerebral perfusion is defined as the steady-state delivery of nutrients and oxygen via blood to brain tissue parenchyma per unit volume and is typically measured in milliliters per 100 g of

tissue per minute. In perfusion MR imaging, however, the term 'perfusion' comprises several tissue hemodynamic parameters (cerebral blood volume – CBV, cerebral blood flow – CBF, and

mean transit time - MTT) that can be derived from the acquired data. In the evaluation of intracranial mass lesions, however, CBV appears to be the most useful parameter.

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1 Slice positioning for the perfusion series (copied to the position of DarkFluid T2).

Perfusion MR imaging methods take advantage of signal changes that accompany the passage of tracer (most commonly gadolinium based MR contrast agents) through the cerebrovascular system. Perfusion imaging can be performed with techniques based on dynamic susceptibility contrast (DSC) or based on vascular permeability. DSC imaging allows approximately 10 MR sections every second and is ideal for rapid dynamic imaging. As the gadolinium contrast enters the circulation, it induces susceptibility changes by way of its paramagnetic properties; this in turn results in shorter T2\* values and significant signal loss. Curves showing intensity changes based on the concentration of gadolinium over time can be generated. The concentration of gadolinium is a direct representation of the capillary density. From this, the relative cerebral blood volume (rCBV) can be determined, which corresponds to the volume of blood within brain tissue. rCBV mirrors the neovascularization associated with tumor angiogenesis; in adults with glial tumors, angiogenesis is highly correlated to tumor grade, and the rCBV of most high-grade glial tumors is greater than that of low grade tumors. Perfusion MR imaging is increasingly being used as a diagnostic and research tool that provides maps of the regional variations in cerebral microvasculature of normal and diseased brains. With relatively short imaging and data processing times and the use of a standard dose of contrast agent, perfusion MR imaging is a promising tool that can easily be incorporated as part of the routine clinical evaluation of intracranial mass lesions. Although still investigational, MR imaging CBV measurements can be used as an adjunct to conventional imaging to help assess the degree of neovascularization in brain tumors, evaluate tumor grading and malignancy, identify tumor-mimicking lesions (such as radiation necrosis, cerebral abscess, and tumefactive demyelinating lesion (TDL)) by demonstrating their lack of angiogenesis, and assess the status of viable tissue surrounding an acute infarct. It must be emphasized, however, that perfusion MR imaging is a relatively new and prom-

ising imaging tool rather than a standard proven technique for tumor grading and staging. In the future, perfusion MR imaging may become useful in the monitoring of treatment, and its results may also potentially serve as an arbiter when determining the efficacy of novel therapeutic agents, especially antiangiogenic therapy.

The DSC-MRI measurements can help investigate hemodynamic abnormalities associated with inflammation, lesion reactivity and vascular compromises. Even a non-enhancing lesion may show high perfusion which suggests inflammatory reactivity that cannot be seen on conventional MRI.

Although brain perfusion has been around for while [2] and its uses and advantages known for more than a decade [2–4], it is not yet widely performed. This could be due to the following reasons:

1. The interpretation/quantification is not well established (or accepted) among radiologists.
2. The post-processing of the images is not yet automated and still needs someone with expertise to perform all or part of the post-processing.
3. The technologists and radiologists assume that it is hard to integrate into the usual protocol.

Brain perfusion can easily be integrated into any brain imaging routine with contrast. Instead of hand injection the contrast bolus should be delivered by a power injector. However, it is at the discretion of the physician to apply contrast media if need be. The perfusion does not add any extra risk to a normal brain MRI examination, as in all these cases the patient would have been given a contrast agent anyway. The perfusion data is acquired during the injection without increasing the amount of Gadolinium contrast. The addition of the perfusion adds about 2 minutes to the examination time. Easy post-processing may add informative maps aiding the radiologists in their diagnoses of various brain lesions.

We have worked on brain perfusion in our clinical setting for the past three

years and have scanned, post-processed and dictated more than 1000 cases. Here we would like to present our method of scanning and post-processing with a few clinical examples to highlight the importance of perfusion in the diagnosis of the lesion in question.

## Methodology

### Scanning

All the brain perfusion studies have been acquired on Siemens MRI scanners and have been post-processed on a Siemens Multi-Modality Work Place (MMWP), with Siemens perfusion evaluation software. The scanners used were: MAGNETOM Symphony with Quantum gradients (software version *syngo* MR A25 and *syngo* MR A30), MAGNETOM Symphony a Tim System (*syngo* MR B15 and *syngo* MR B17), MAGNETOM Sonata (*syngo* MR A25), MAGNETOM Avanto (*syngo* MR B15 and *syngo* MR B17), all 1.5T and the 3T MAGNETOM Verio (*syngo* MR B15 and *syngo* MR B17).

The perfusion was done as part of the routine (with contrast) brain examination for patients who were scheduled for surgery or at the request of a radiologist. Our routine brain exam consists of sagittal T1 (TSE), axial T2 (TSE), axial FLAIR (TSE), axial EPI diffusion and post-contrast axial MPRAGE T1. The perfusion series uses the sequence *ep2d\_perf* that can be found in the Siemens protocol tree under head-Advance-Diffusion & Perfusion. We modified the Siemens standard protocol slightly to suite the rest of our protocols to match primarily the slice thickness, slice gap and field-of-view (FOV).

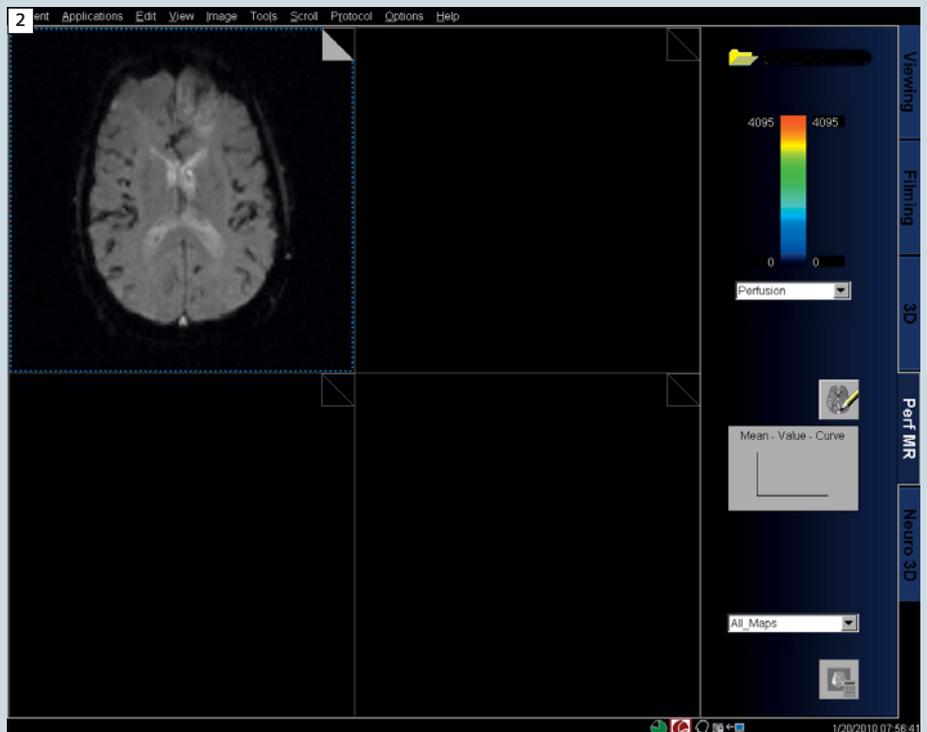
The following are the steps to perform a brain perfusion study on a Siemens MR scanner:

- Make sure the patient has a good intra-venous line (IV) with a needle gauge of 18 or 20. Use the antecubital veins and avoid more peripheral placement of the needle.
- Hook the patient's IV to an injector and set the injection rate to 4 ml per second. A normal contrast dose of 0.1 mM/kg should be used.

- Make sure the IV is good and shows no resistance to flow.
- Start the routine exam, and insert the perfusion procedure just before the post-contrast T1.
- The perfusion imaging slices should have the same **positioning, thickness and gap** as the axial FLAIR or T2 sequences to facilitate a direct comparison of the perfusion results with other pre- and post-contrast images (Fig. 1).
- Make sure that both the lesion and cortical white matter are covered.
- The phase encoding direction needs to be anterior-posterior (A/P) to reduce susceptibility artifacts.

After the pre-contrast portion of the brain exam is done, be ready with the injection: start the scan and inject the contrast at the 8<sup>th</sup> measurement. The scan has 50 time points (measurements) of ~2 s each resulting in total time just below 2 min.

Send the main series to the workstation where you want to do the post-processing of the images.



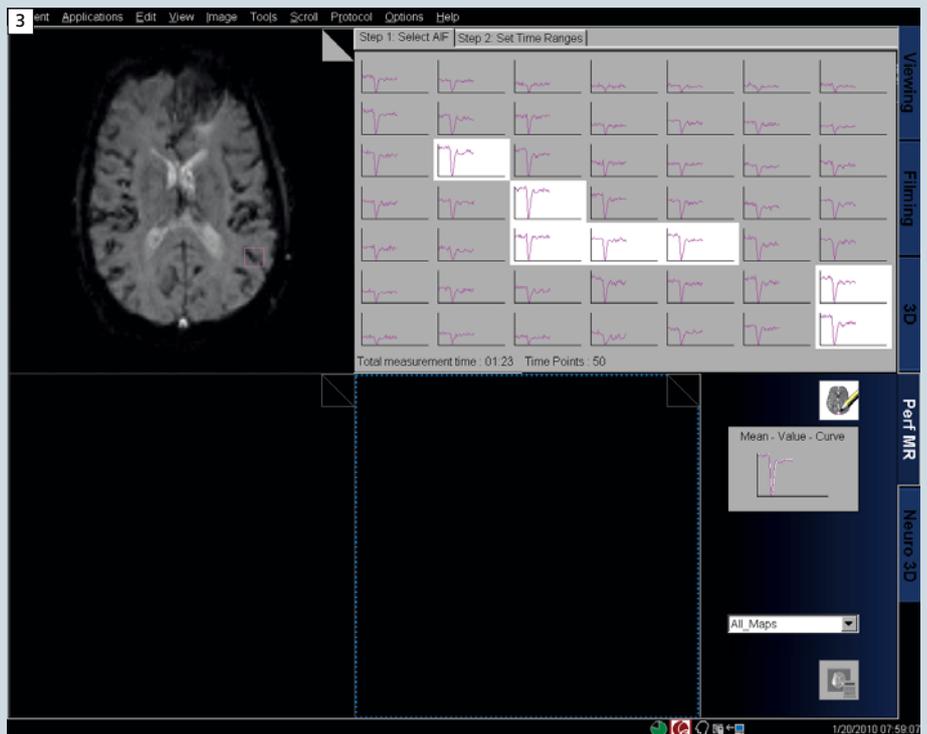
**2** Opening page of the perfusion application. The perfusion series has been dropped and can be seen in the first quadrant (top left).

### Post-Processing

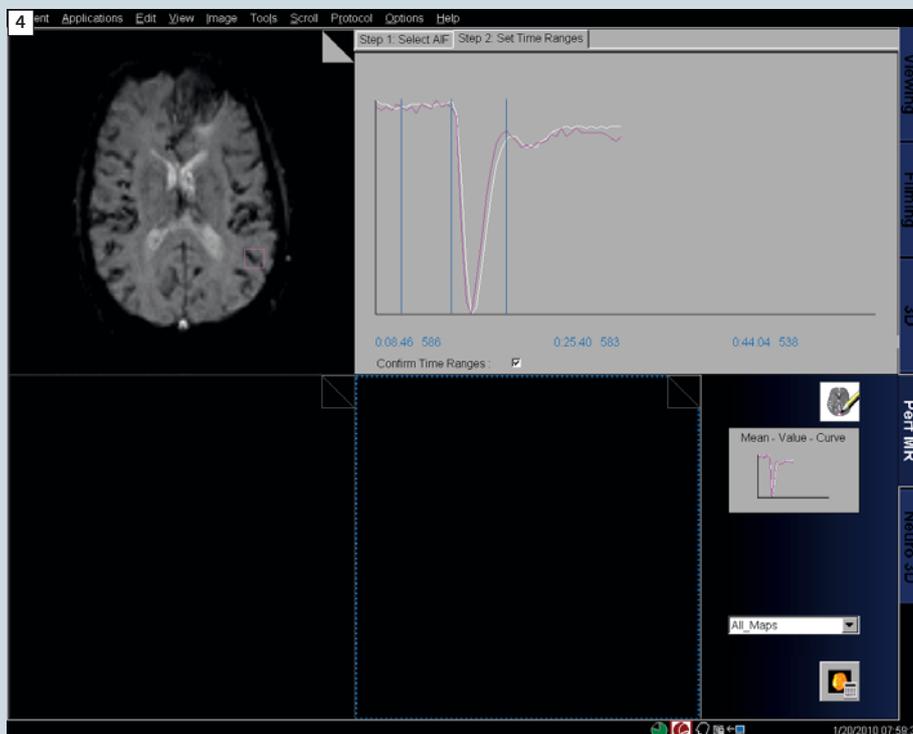
- On the Siemens workstation (MMWP or Leonardo), open the perfusion application (Application-Perfusion).
- Open the Patient Browser and load the main perfusion series into the Perfusion Page (Fig. 2).
- Click on the images and page through to get to the slice where you can see the area of interest (tumors etc.).
- Identify an artery on the same slice.
- Click on the small AIF icon:

 A square appears on the image. Place the square on the artery (Fig. 3).

- On the right side of the screen (Fig. 3), select AIF, by choosing the best time graphs, the ones with significant signal drop (highlighted squares). Do so for 4 or more time-points, hold the Contr.-key while clicking with the left mouse-button.

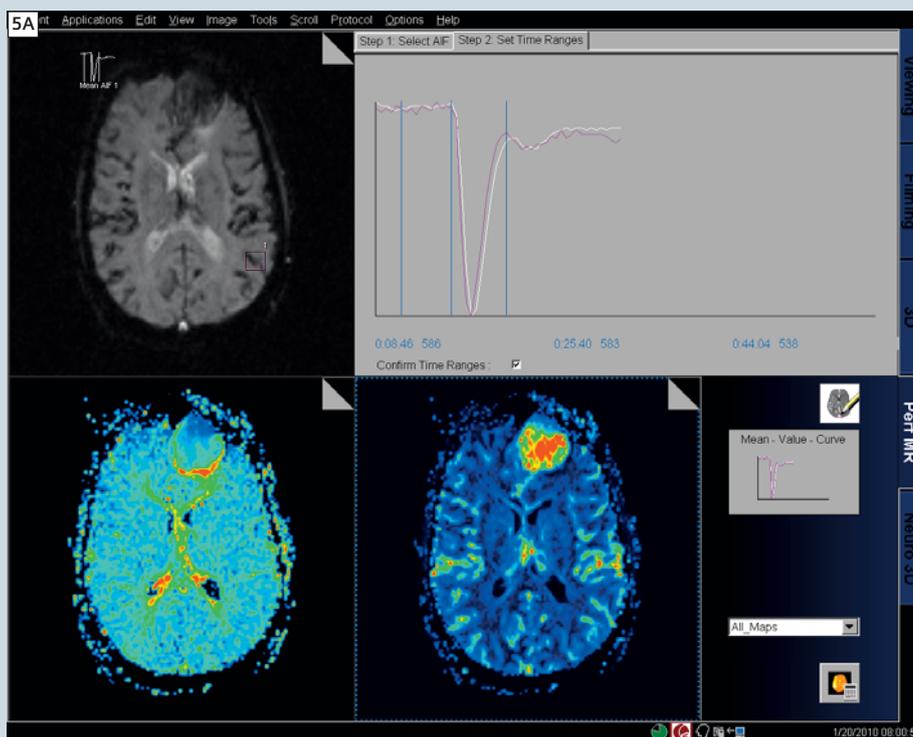


**3** The arterial input function (AIF) square is shown on a slice of the perfusion image data, with the resulting 9x9 pixels time points on the right side. The highlighted region-of-interest (ROI) is used to calculate the AIF from.



**4** The resulted AIF, with the three time points properly shown. The first one is at the baseline, second at the start of the drop and the third at the end of the drop (peak of recovery).

- When done, click on the second tab: Step 2: Set Time Ranges (Fig. 4). Move the three time-lines, so that the first one is at the start of the baseline, the second one at the beginning of the drop (Gad entry) and the third one at the peak of the recovery, as shown in Figure 4. Then click the check box 'Confirm Time Ranges'.
- Make sure the selector at the lower-right side of screen is on 'All Maps'.
- Click on the color calculator/brain icon  at the bottom-right corner of the screen. If the icon is dimmed (grayed out) the time selection has not been done yet. The calculation takes about 20–30 seconds.



**5A** Figure shows the perfusion screen, after the calculation is done. (5A) The rCBF is displayed in the fourth quadrant (lower right) and the TTP is displayed in 3<sup>rd</sup> quadrant (lower left).

Once the calculation is done, the rCBV (relative cerebral blood volume) and rCBF (relative cerebral blood flow) color images are displayed in the 4<sup>th</sup> quadrant, of the screen, as shown in figure 5 (A and B). Toggle between series using the '4' and '5' keys on the numerical key pad (on right of keyboard). The third quadrant shows the MTT (mean transit time) and TTP (time-to-peak) maps. We don't bother with these.

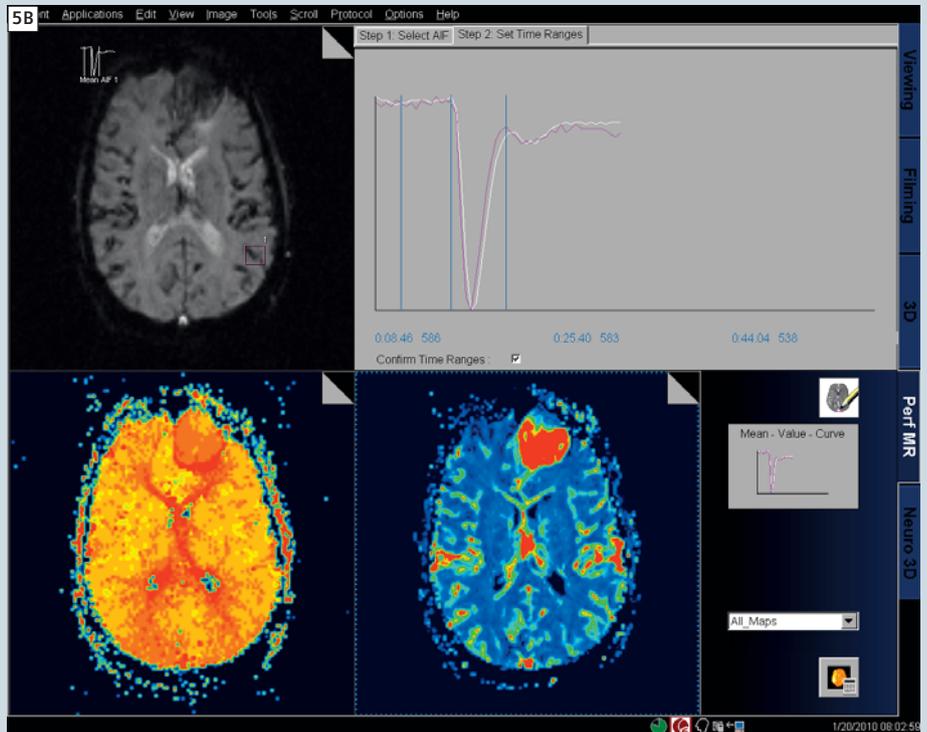
- In the 4<sup>th</sup> quadrant, i.e. the bottom right segment, select series (right mouse button), adjust the windowing (center mouse button) and save as new series (from the top menu, File-Save As... (e.g. call them **CBV\_color** or **CBF\_color** depending on which one was selected).

These are just the color maps but the pixel values are arbitrary.

**Normalization of pixel values**

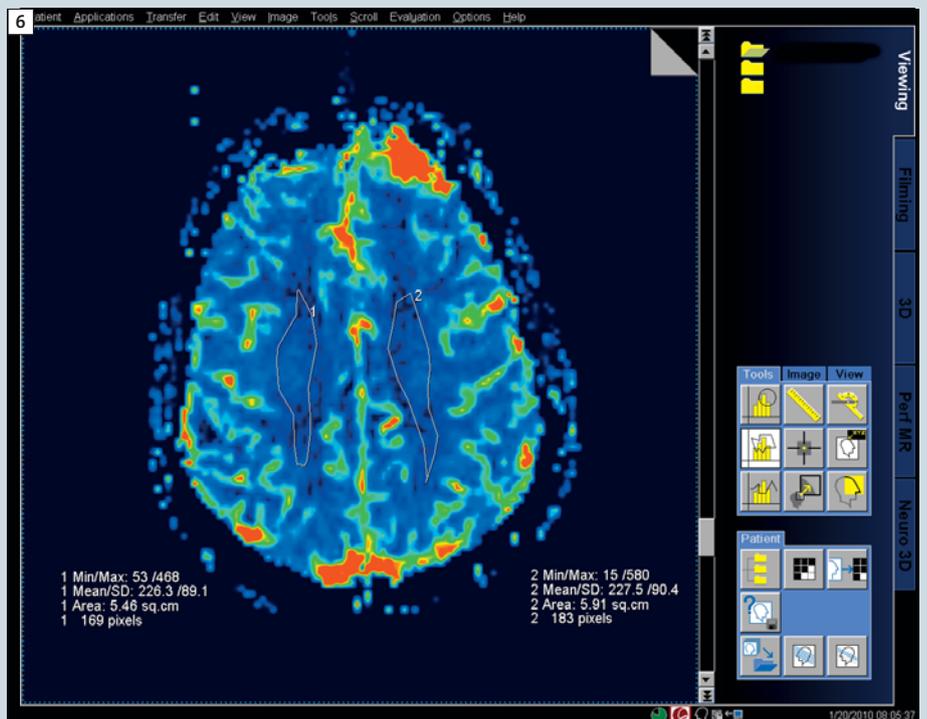
To normalize the values:

- Go to the Viewing card (right side tabs) and open the series 'CBV\_color'.
- Scroll to the top of the brain where you can see the cortical white matter without any distortions.

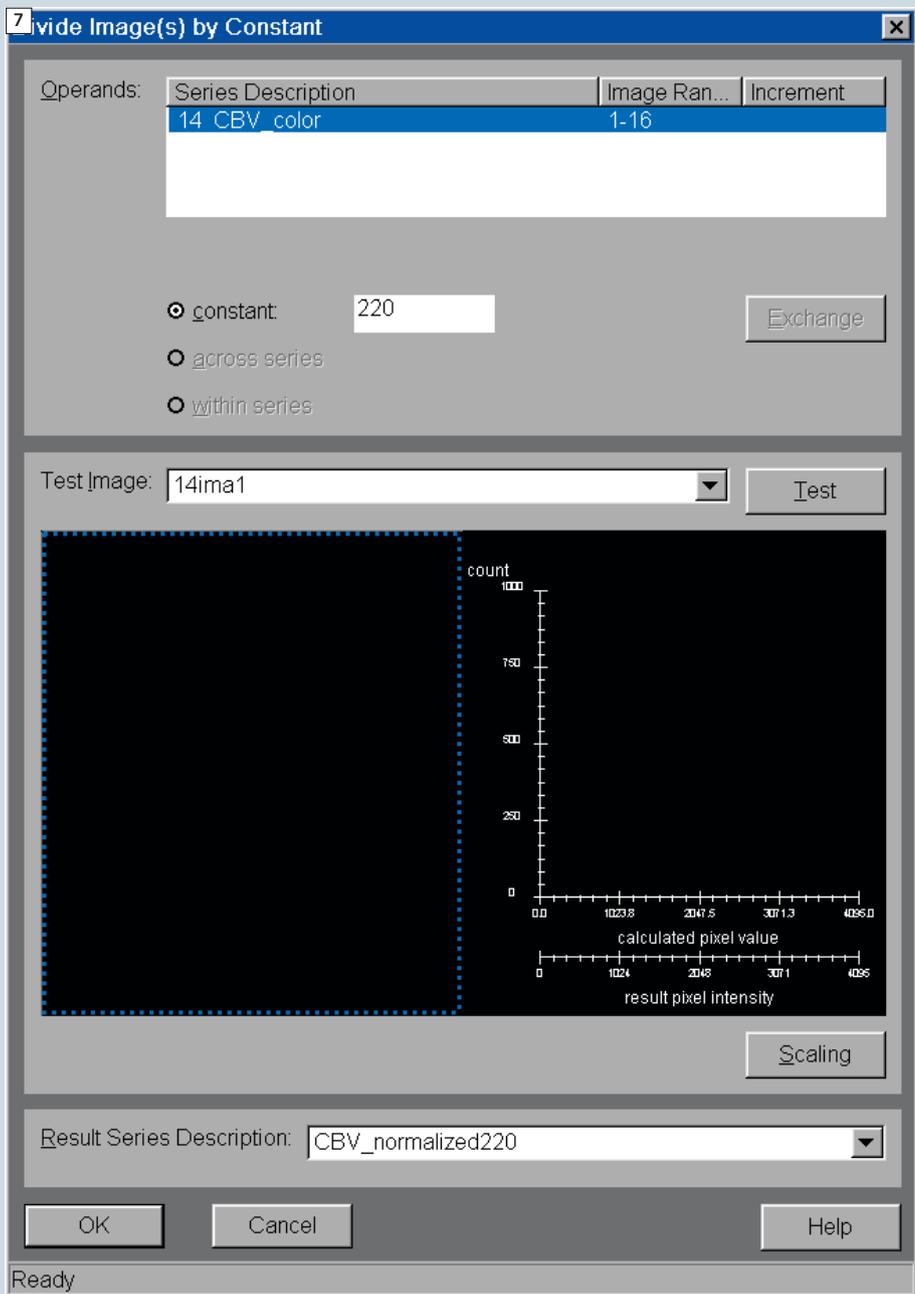


**5B** The rCBV is displayed in the fourth quadrant (lower right) and the MTT is displayed in 3<sup>rd</sup> quadrant (lower left).

- Using the free hand drawing (right side panel), draw an enclosure (Fig. 6), which only contains healthy white matter, one on each side, if possible, and on two slices, if possible.
- Read the mean signal values and calculate their average (avg) mean value (adding all the values and divide by the number of samples used).
- Select the whole series (right mouse button). From the top menu choose 'Evaluation- Dynamic Analysis – Divide...'



**6** Typical region selection for the cortical white matter tissue, to find the average healthy white matter intensity.



- In the new window (Fig. 7) enter the mean value (avg from above) as the constant and rename the final series to **CBV\_normalized\_avg** under 'Result Series Description'. Press ok.
- Open the browser and select the 'CBV\_color' series.
- From the Application tab, choose: MR – DICOM – Save as RGB. This creates a series automatically named 'CBV\_color\_RGB', adding ' \_RGB' to the original series name. This makes the CBV\_color series RGB-color coded so that it can be seen in color on PACS workstations.
- Do the same for 'CBF\_color'.

7 The dialog box which opens for dividing the whole rCBV by a number (average Cortical WM).

## Discussion

Following the above procedure we have done many brain perfusion studies and have used them to grade tumors. The idea of having the color maps and the normalized version is that the normalized version appears only in gray scale on PACS stations, but its pixel intensities

have CBV values normalized to white matter. By simultaneously displaying and correlating the color CBV images with the normalized ones, the radiologist is able to see the tissues color coded and can read the corresponding perfusion values with respect to healthy white

matter (normalized value). In the literature describing a few studies with an aggressive tumor the perfusion ratio (with respect to white matter) was above 2.5 [5]. By using this method a radiologist can evaluate and grade a tumor more quantitatively.

## Case reports

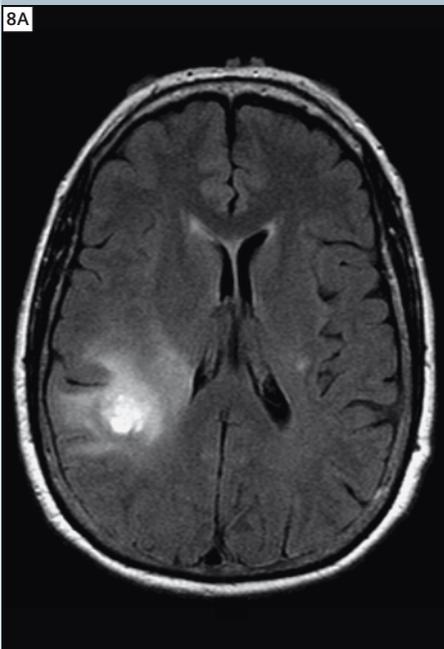
To illustrate the usefulness of perfusion imaging in clinical practice, here are four clinical examples from our practice:

### Case 1

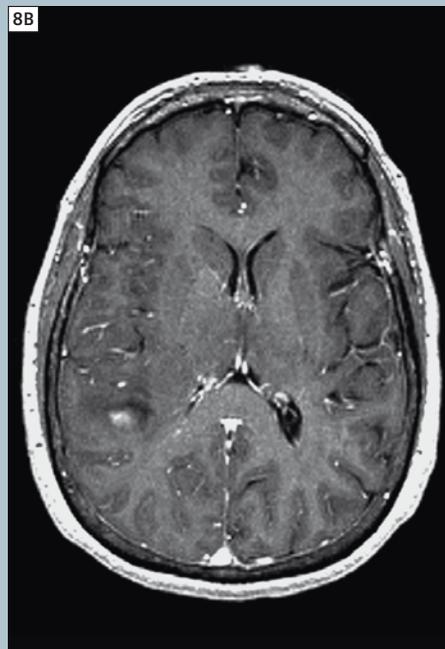
A 64-year-old female with a history of brain tumor received radiation and chemotherapy treatment a few months prior to our examination. The initial MRI showed abnormal signal on FLAIR (IR T2), but the T1w post-contrast

showed no enhancement. This pointed to a low grade tumor. A follow-up MRI with perfusion was performed, which again showed abnormal hyperintensity on FLAIR (Fig. 8A) and no gadolinium enhancement (Fig. 8B), but the perfu-

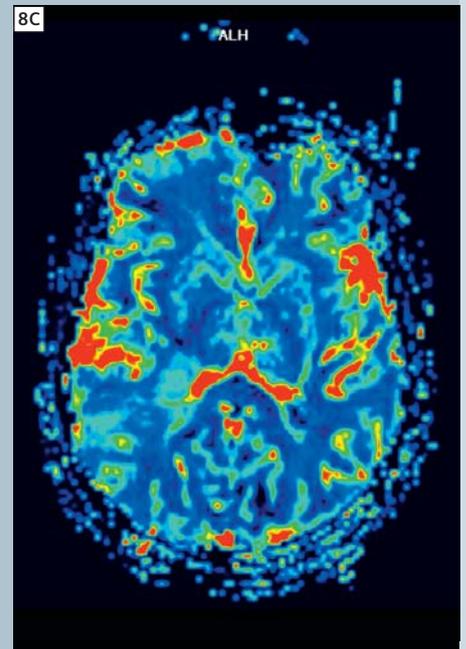
sion images (rCBV) (Fig. 8C) showed highly perfused tissues pointing to a high grade neoplasm, which was subsequently resected. Histology confirmed high grade astrocytoma.



8A Axial FLAIR



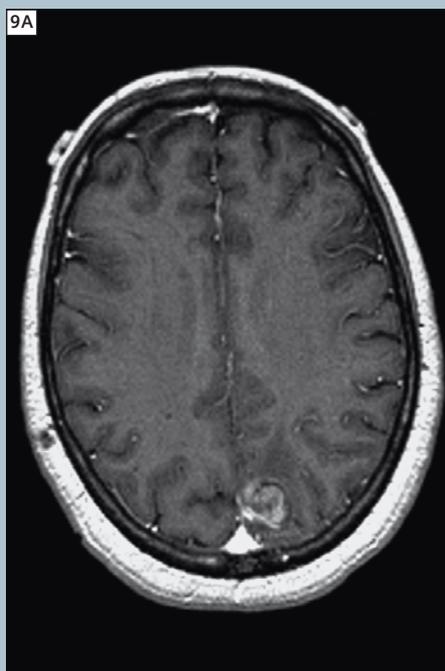
8B Axial post T1



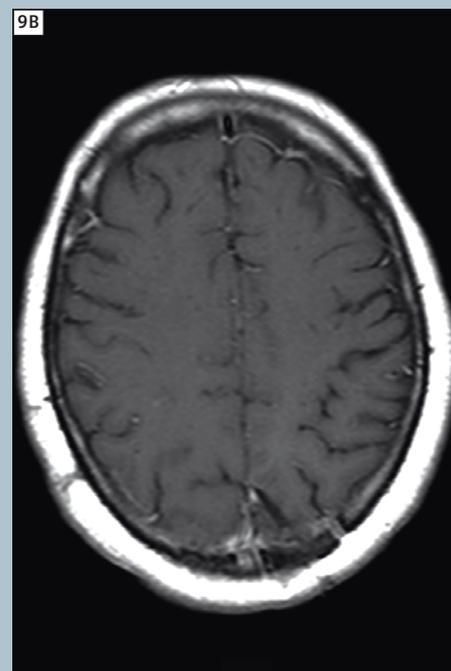
8C Perfusion map CBV

## Case 2

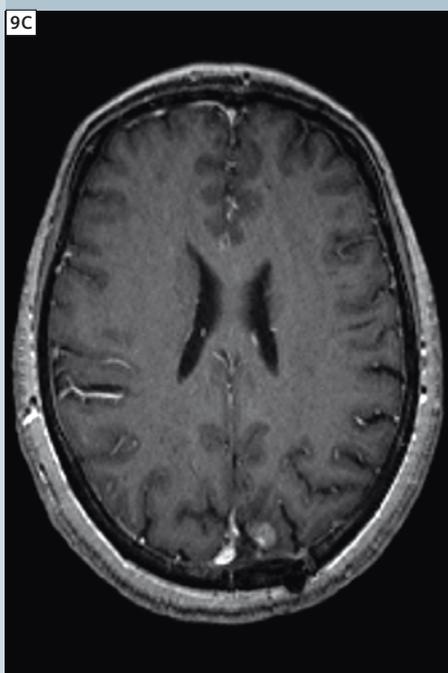
A 60-year-old female with history of metastatic lung cancer, presented with metastatic nodule in the left occipital lobe. She underwent craniotomy followed by postoperative radiotherapy to the surgical bed. The one year follow-up brain MRI showed minimal enhancement on post-contrast MRI. The two year follow-up showed a nodular mass, which further grew on short term follow-up. The diagnosis could be either new tumor growth or radiation necrosis. The low signal of rCBV in her perfusion examination pointed toward radiation necrosis rather than tumor re-growth. The enhancing part was subsequently excised and pathology confirmed radiation necrosis.



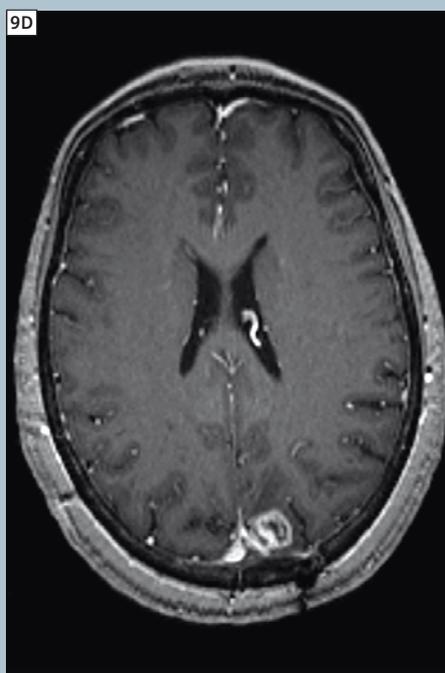
**9A** Axial post T1 (pre-surgical)



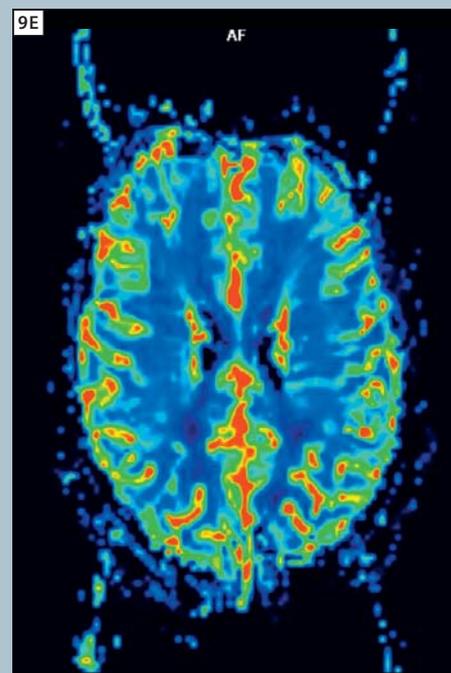
**9B** Axial post T1 (one year post surgery)



**9C** Axial post T1 (two years post surgery)



**9D** Axial post T1  
(2 years and 2 months post surgery)



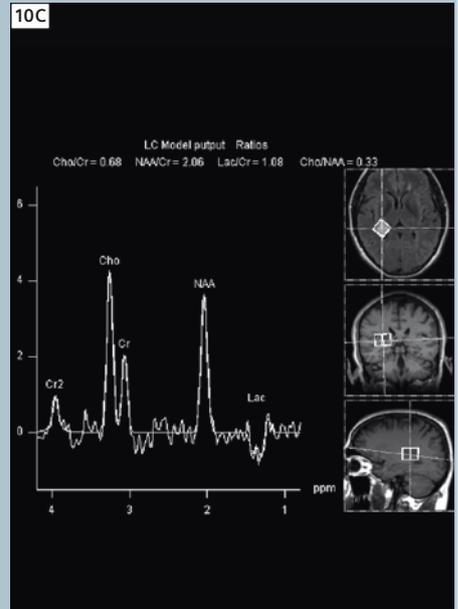
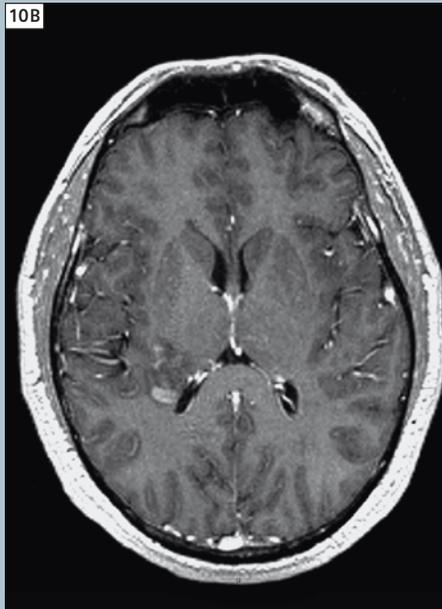
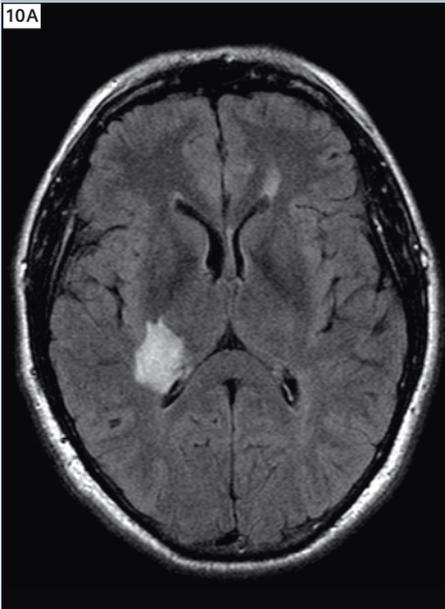
**9E** Axial perfusion map CBV  
(2 years and 2 months post surgery)

### Case 3

The routine MRI of a 48-year-old right-handed man showed a lesion at the right thalamus suspected of low grade glioma. Subsequent imaging showed a lesion involving the right posterolateral thalamus posterior to the periven-

tricular white matter, which had features suggestive of tumoractive multiple sclerosis (MS), but the possibility of primary brain neoplasm could not be excluded, especially as the MR spectroscopy (MRS) showed elevated

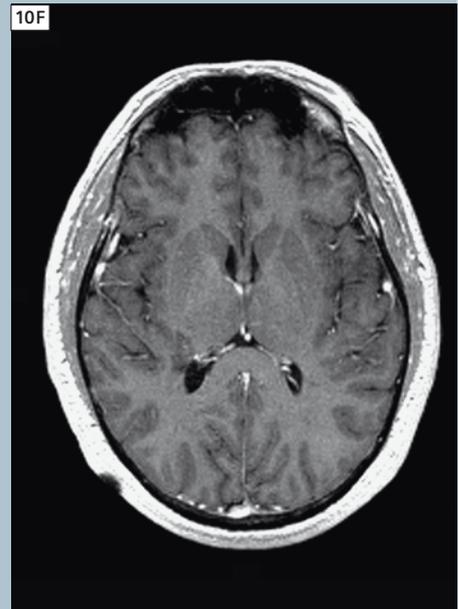
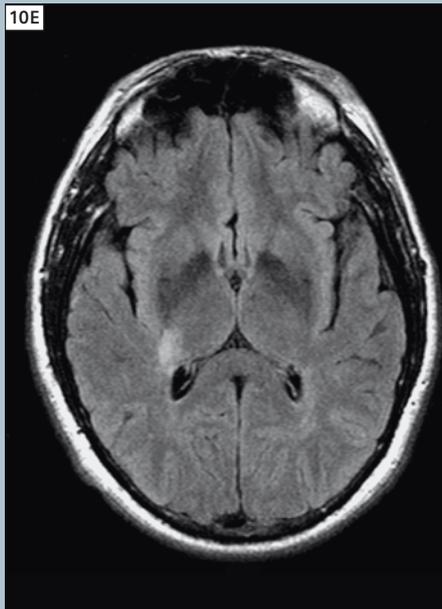
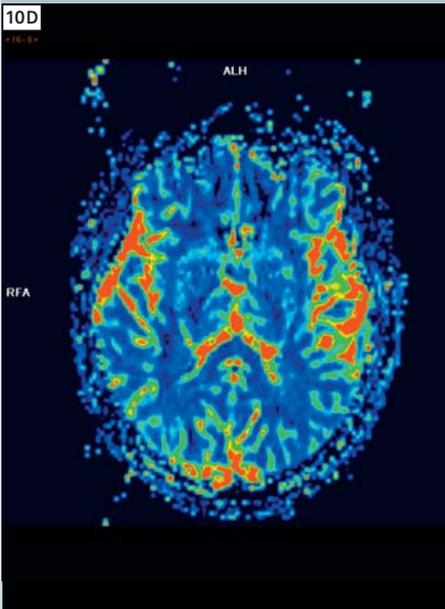
choline signal. The perfusion protocol was performed and both the rCBV and rCBF showed low values (close to those of normal white matter). That pointed to MS with a low possibility of an additional primary brain neoplasm.



10A Axial FLAIR

10B Axial post T1

10C Single Voxel Spectroscopy



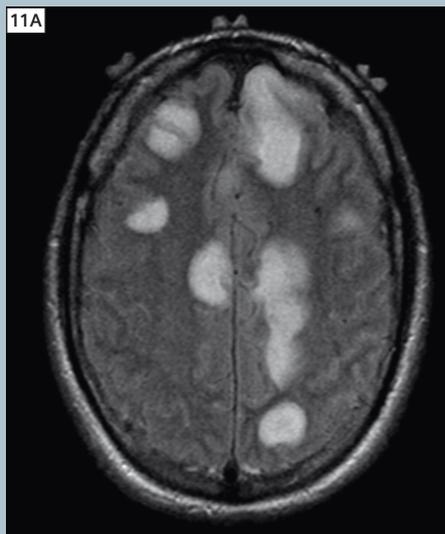
10D Axial perfusion map CBV

10E Follow-up axial FLAIR

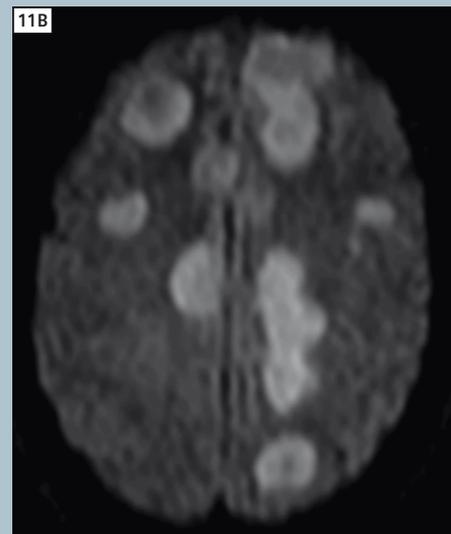
10F Follow-up axial post T1

## Case 4

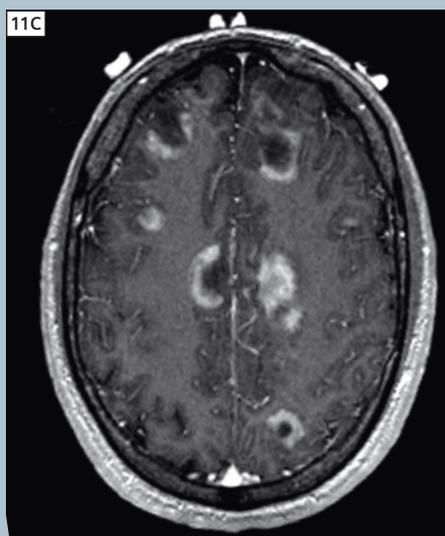
A 31-year-old HIV-positive male with history of head trauma, and drug abuse, was admitted to emergency with chief complaint of right side weakness and confusion. The initial CT exam of the brain indicated findings consistent with multiple, predominantly cortically based infarcts in the bilateral frontal and temporal lobes. No hemorrhage was seen. The following MRI showed multiple areas of abnormal T2 signal. The diffusion images showed T2 shine through effect. There was no significant mass effect from these lesions. The findings were suggestive of a diagnosis of acute disseminating encephalomyelitis or tumefactive MS. No sign of hemorrhage was observed. On the CBV images obtained from perfusion, the abnormal areas appeared dark, indicating low perfusion. In view of the immunosuppressed condition of the patient, craniotomy and biopsy was performed to exclude opportunistic infections and neoplasms. Surgical pathology confirmed the diagnosis of acute disseminating encephalomyelitis. Follow-up MRI demonstrated slight regression of the lesions.



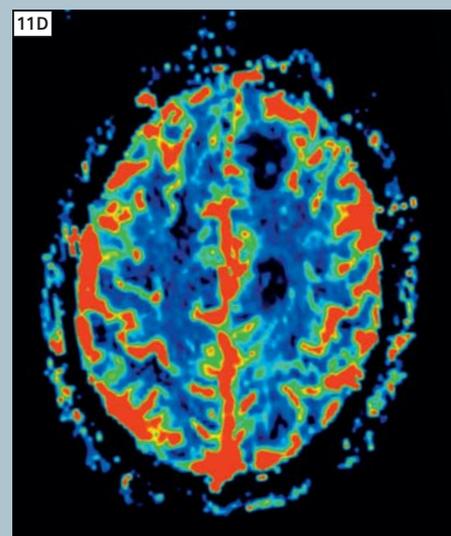
11A Axial FLAIR



11B Axial diffusion-weighted imaging (b=1000)



11C Axial post T1



11D Perfusion map CBV

### References

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- 2 C.L. Partain. "Brain Perfusion Imaging Using Magnetic Resonance". Editorial *J Mag Reson Imaging*, 22 (2005) 691.
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### Contact

Nader Binesh, Ph.D.  
MR Physicist  
Cedars-Sinai Medical Center  
8700 Beverly Boulevard  
Los Angeles, California 90048  
USA  
Phone: +1 310 423 4056  
bineshn@cshs.org