Cerebral volume measurement by flat panel detector in the angiography suite: optimisation of injection protocols to reach the steady state

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Purpose

Endovascular treatment is a promising approach for early stroke therapy (1). However selecting the right acute ischemic stroke patients eligible for revascularization therapy can be challenging (2). Cerebral blood volume (CBV) anomalies are correlated to definitive lesions (3). The extent of pre-intervention CBV abnormality is a strong predictor of functional outcomes following endovascular stroke therapy (4).

Advanced modality imaging evaluation in acute ischemic stroke may lead to delay in endovascular reperfusion therapy. Sheth et al. showed that stroke patients selected with non contrast CT scan had significantly lower median times to groin puncture, nearly twice shorter compared with perfusion CT scan and MRI (5).

Recently the feasibility of Flat panel detector CT (FPCT) CBV measurement within the angiographic suite has been described in acute stroke patients (6, 7). This technique requires a steady state of brain parenchyma enhancement during whole acquisition (8) (Fig 1-2). This steady state is a major parameter to ensure the reliability of CBV assessment.

CBV measurement using C-Arm CT is not an everyday tool, and the acquisition technique is not yet codified. Various protocols have been described, using either venous or arterial injections. The reality of the steady state during acquisition is usually assumed but not verified. The purpose of this study is to determine a standard injection protocol ensuring enough steady state time for a reliable CBV measurement.

Images for this section:

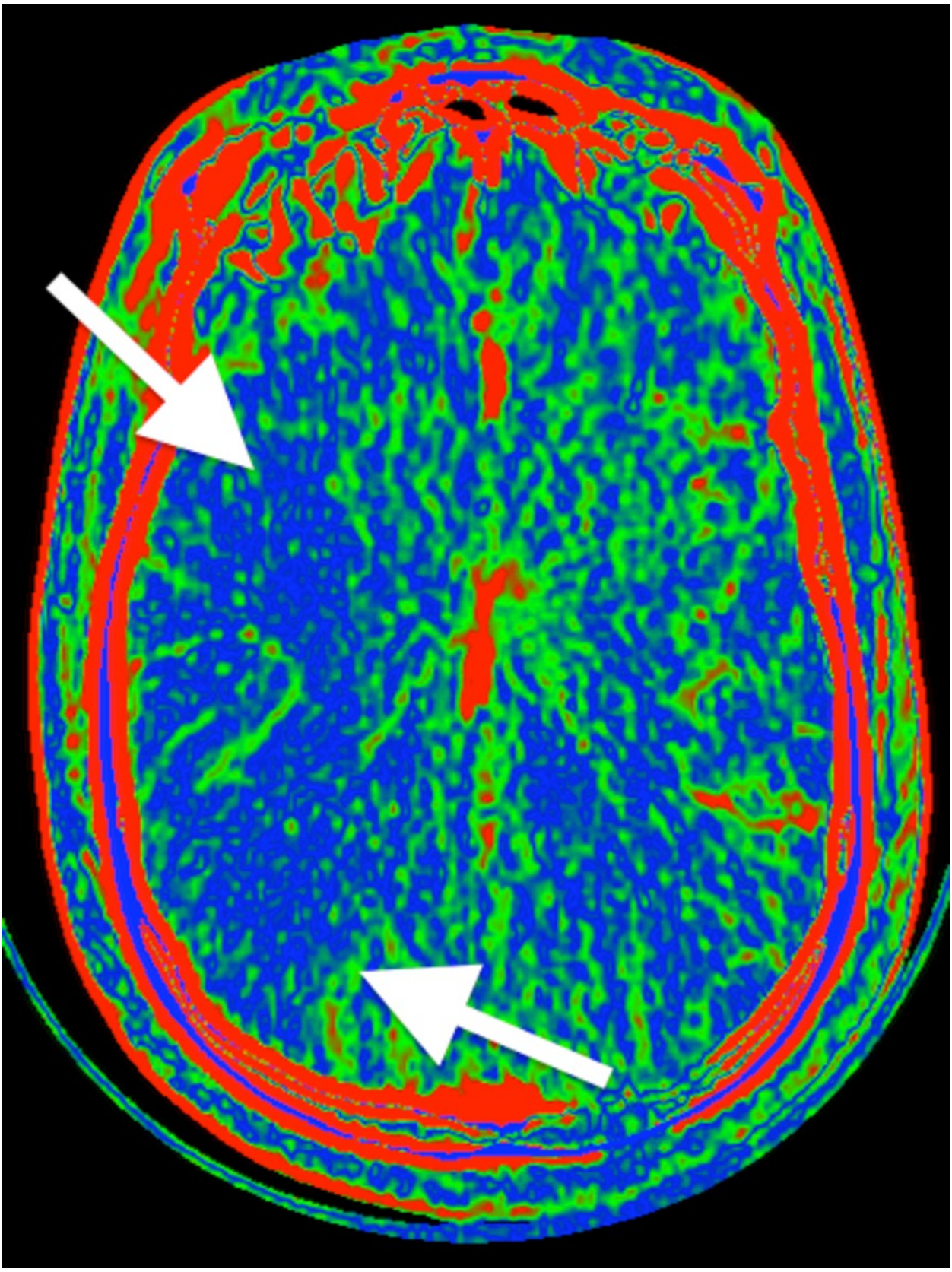

Fig. 1: A 44-year-old patient presenting with left acute hemiplegia. Intracranial bleeding was ruled out by a CT scan and then patient was admitted in the angiographic suite for endovascular early stroke therapy. Preinterventional FPCT CBV measurement showed decreased CBV in the right middle cerebral artery territory (arrows).

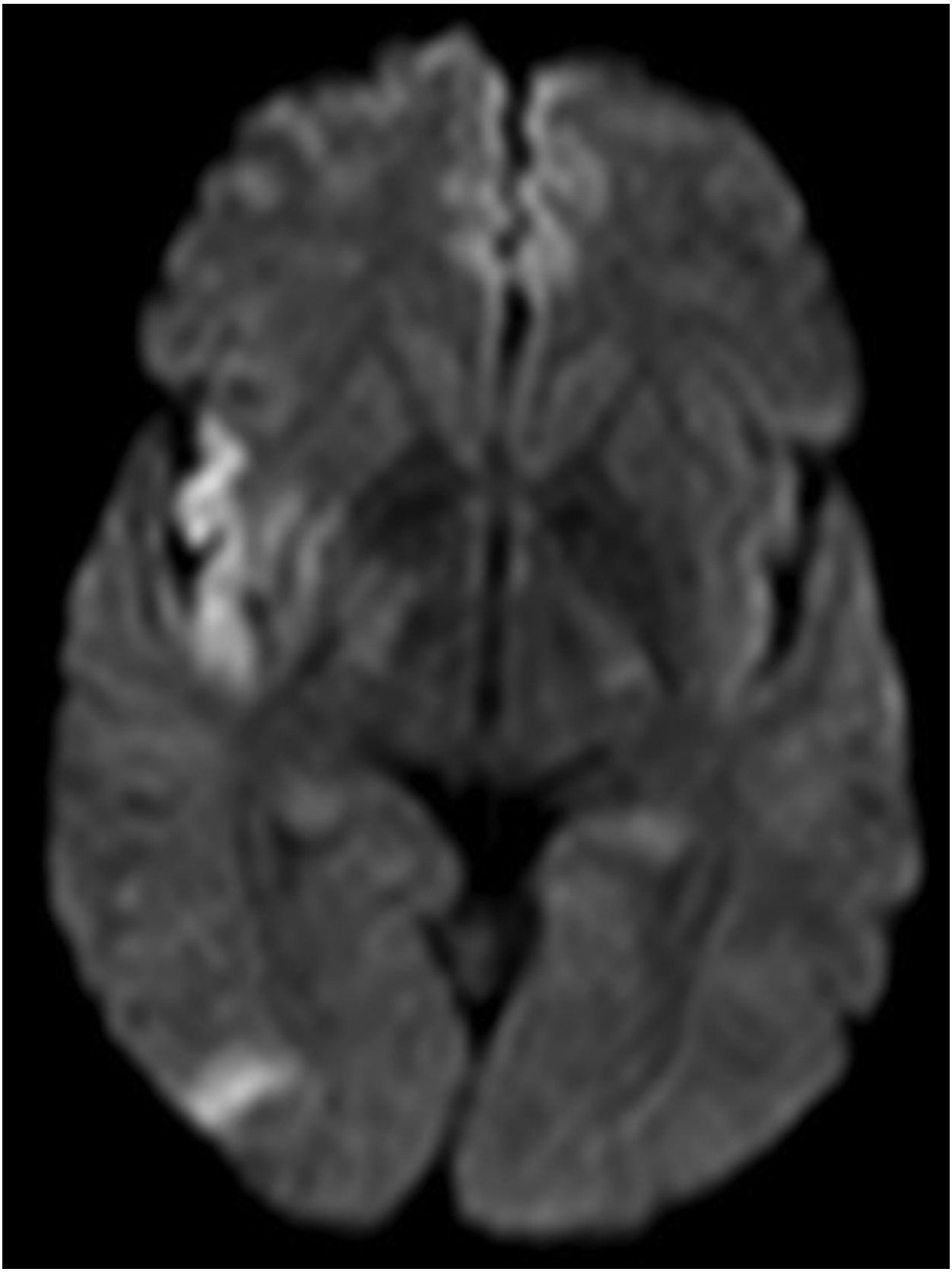

Fig. 2: 24 hours control MRI after successful thrombectomy confirms small cortical infarctions, restricted in the areas of decreased CBV.

Methods and Materials

Patient characteristics

Between May 2012 and January 2013, 24 patients (14 women, 10 men; age range, 19 - 84 years; median, 39 years) referred for endovascular treatment were prospectively enrolled for this study performed according to the guidelines of our institution, informed consent was obtained for each procedure.

Perfusion study was acquired in the angiographic suite during 10 brain arteriovenous malformation endovascular treatments and 14 intracranial aneurysm flow-diverter stent-assisted treatments.

FPCT CBV measurement

Both endovascular treatment and perfusion study were performed on a biplan angiographic system (Allura Xper, Philips Healthcare, Best, the Netherlands) under general anesthesia. FPCT CBV was assessed before embolization for brain AVM and after stent delivery for aneurysms.

Perfusion protocol consisted first in a test acquisition in order to obtain time intensity curves of tissue enhancement in brain parenchyma. It corresponded to a 3 images per second subtracted postero-anterior fluoroscopic acquisition during 30 seconds. It was initiated after an 8 second delay for central injections and 12 second delay for peripheral injections, in order to minimize the X-ray dose.

Secondly FPCT CBV measurement was performed as previously reported (9), but with a 5 second rotation time and a tailored acquisition delay from injection calculated from test acquisition.

Injection protocols

Injection protocols were the same for test acquisition and for CBV measurement. Contrast media injections were performed either through a 4F pigtail intra-atrial venous catheter for 20 patients or through a peripheral cubital acces for 4 patients. We used 72 mL of iodixanol (Visipaque 270, GE Healthcare, Mississauga, Canada) at an injection rate of 4 mL/s, followed by a 20 or 72 mL saline flush at the same rate.

Initially, we used a literature inspired protocol (6), consisting in the injection of the same amount of contrast media than saline flush (72/72 protocol). From preliminary results this protocol was adjusted by decreasing saline flush volume to 20 mL for the following patients (72/20 protocol).

Post processing

Data were analyzed by using commercially available software, *2D Perfusion* (Philips Healthcare, Best, the Netherlands) and exported to *Excel* software (Microsoft, Redmond, Washington, USA). From a large region of interest drawn in the non-pathological hemisphere and avoiding major vessels we have determined time attenuation curves with a 0.33 second time resolution (Fig 3). As steady state required strictness for the FPCT CBV measurement has not been previously evaluated in the literature we have arbitrarily chosen a 15% tolerance threshold from peak attenuation value (fig 4). From this was measured the steady state length and the delay from injection to the steady state's beginning.

Raw data from test injections (i.e. digital subtraction angiography) were secondarily analyzed by two neuroradiologists (20 and 5 years of experience). They determined delay from injection to full opacification of venous sinuses, this is called "bolus watching" technique and it would be related the steady state's beginning according to some authors (6, 7, 10)(fig 5). When using "bolus watching" technique, the rotational acquisition is manually initiated after contrast agent injection when the superior sagittal sinus is opacified.

Statistical analysis

Statistical analysis was performed using commercial statistical software *SPSS* (version 12.0, Statistical Package for the Social Science, Chicago, IL). Correlations between readers using "bolus watching" technique and the measured steady state delay from time density curves were performed using Spearman correlation coefficient. Steady state's average delay from "bolus watching" and from time density curves were compared using Wilcoxon rank sum test. Average steady state's length from different injection protcols were compared using Mann-Whitney *U* test.

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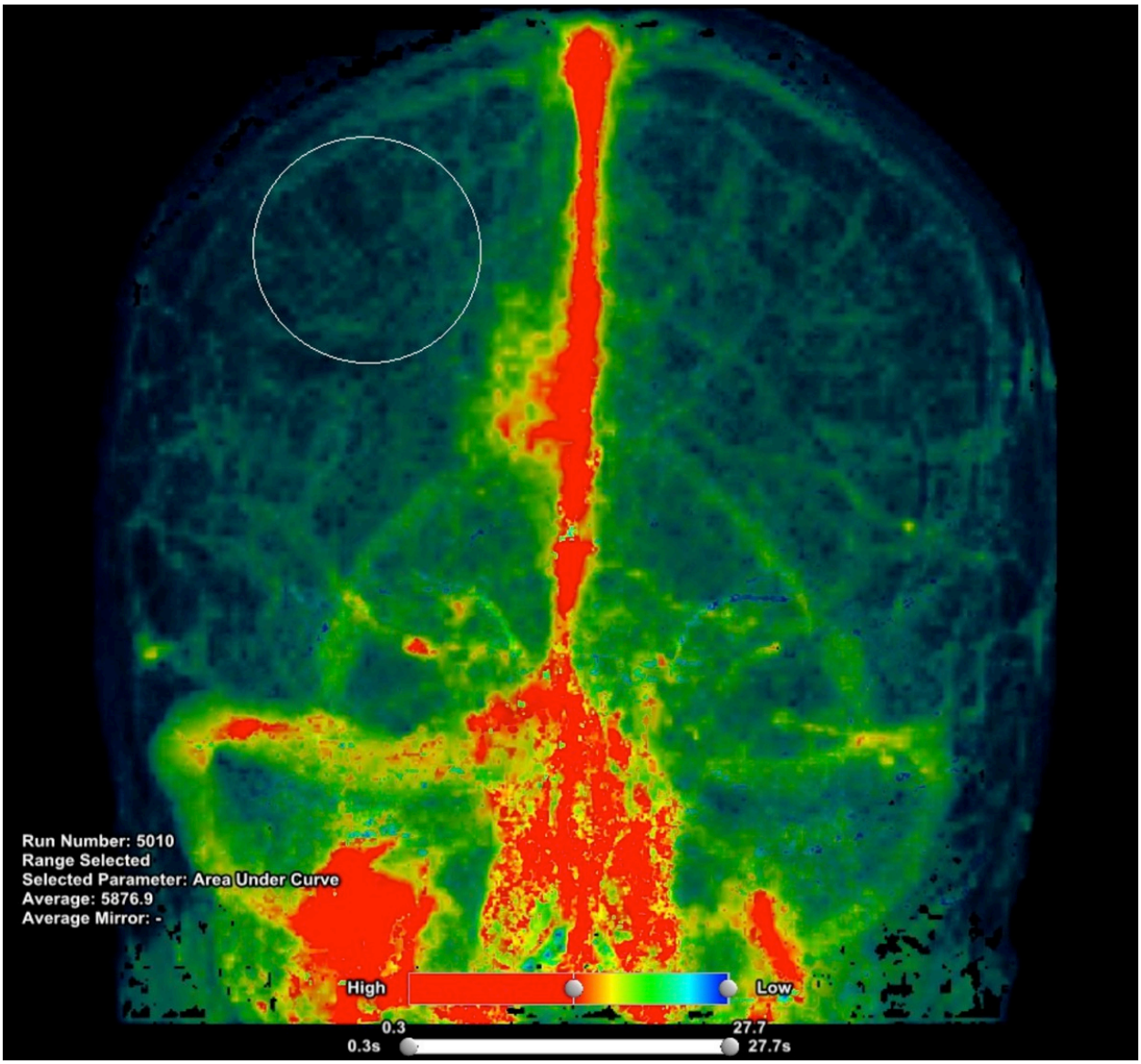

Fig. 3: A circle region of interest is drawn in a brain antero-posterior projection to obtain time intensity curves thanks to the 2D perfusion software. From this, steady state's characteristics will be determined.

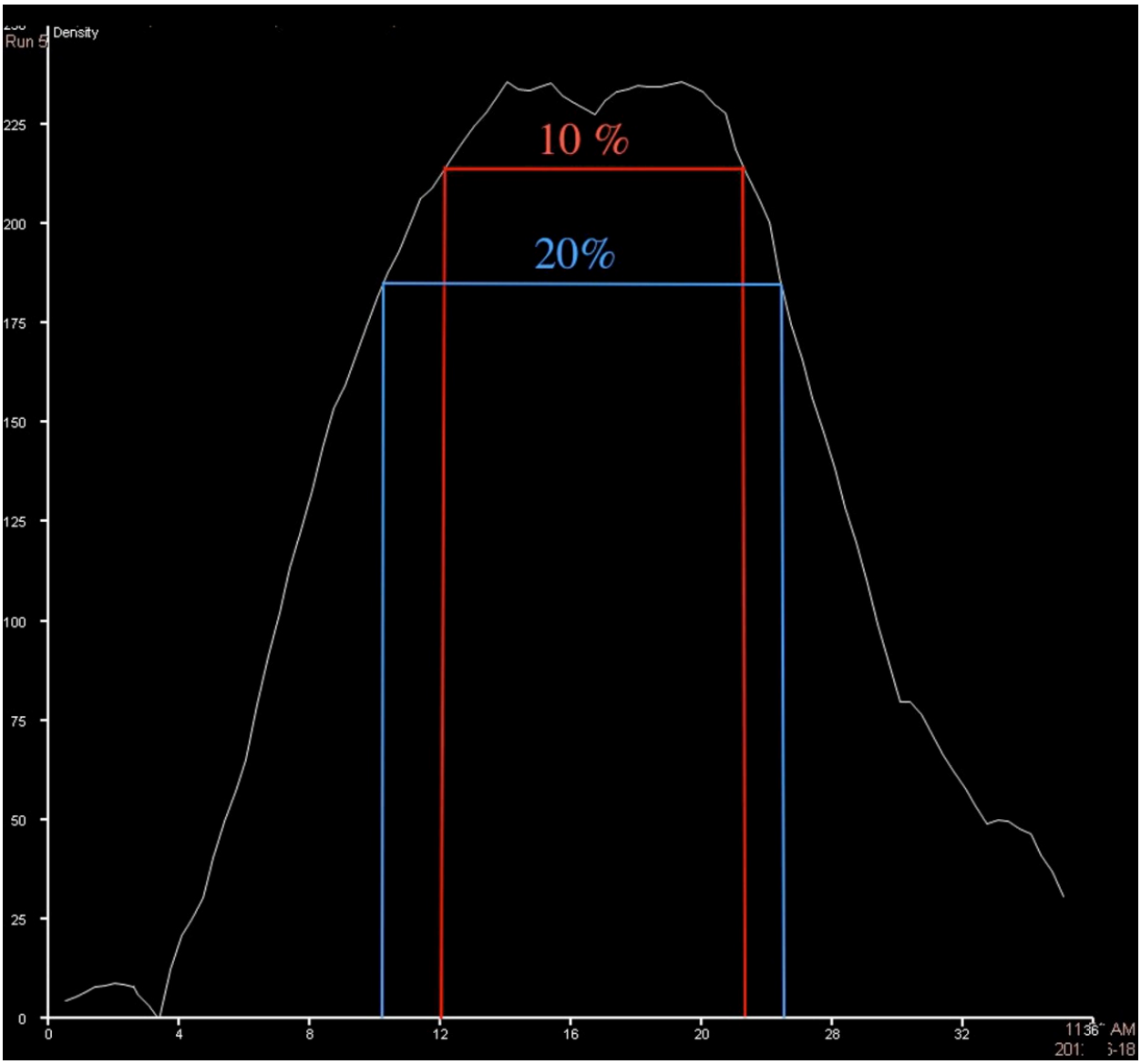

Fig. 4: Illustration of steady state's length measurement from peak value of time intensity curve. For example, here with a 10 % threshold we would obtain 9.6 seconds and 12.2 seconds with a 20 % threshold.

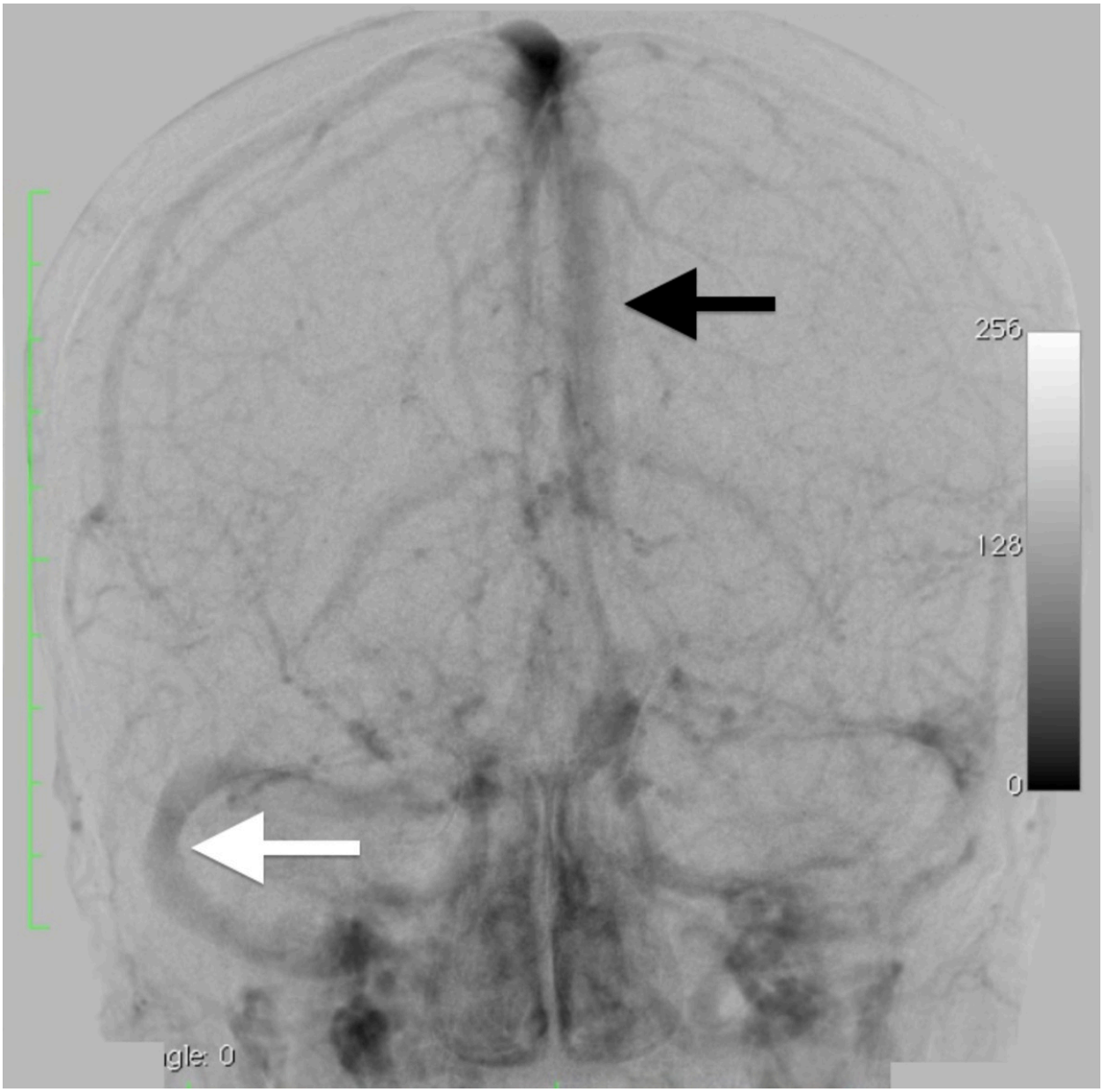

Fig. 5: Homogeneous opacification of venous sinuses is considered by some authors to be the reflect of the steady state's beginning. Superior sagittal sinus (black arrow) and lateral sinus (white arrow) opacified.

Results

Time intensity curves analyze was possible in every case. 20 patients were explored using central venous injections; 10 with the 72/72 protocol and 10 with the 72/20 protocol. 4 patients were explored using peripheral injections (Table 1).

	Number of patients	Average age	Aneurysm / AVM
Central 72/72	10	46	7 / 3
Central 72/20	10	35	6 / 4
Peripheral 72/72	4	43	1 / 3

Table 1. Injection protocols.

There were no statistical differences between mean peak values of the three different protocols (Central 72/72 = 228, Central 72/20 = 196, Peripheral 72/72 = 201).

With central injections, mean lengths of the steady state were respectively 9.2 +/- 1.5 seconds (range 5.9 - 11.2) and 9.9 +/- 1.3 seconds (range 7.6 - 11.9) for the 72/72 and 72/20 protocols. With peripheral injections it was 8.2 +/- 0.9 seconds (range 6.9 - 8.9).

Central venous injections with the 72/20 protocol are associated with a longest mean steady state. Mean differences are 0.7 second compared with the 72/72 protocol, and 1.7 second compared with peripheral injections, but no statistical difference has been shown. The central 72/20 protocol is also associated with less timing variation from injection to steady state, especially when compared with peripheral injections. Mean delays are respectively 21.5 seconds versus 28.4 seconds and standard deviations are 2.0 seconds versus 5.9 seconds.

When using peripheral access, the delay between injection and the beginning of the steady state was nearly 7 seconds later than with central injections. This is logical and corresponds to the time the contrast agent goes from the forearm to the right atrium (Table 2).

	Length	Delay	Peak Value
Central 72/20	9.9 +/- 1.3 s	21.5 +/- 2.0 s	196
Central 72/72	9.2 +/- 1.5 s	20.0 +/- 2.8 s	228

Peripheral 72/72	8.2 +/- 0.9 s	27.2 +/- 5.0 s	201

Table 2. Characteristics of the steady state.

When considering central venous injections, there was a significant agreement between the two readers regarding the timing determination of full opacification of venous sinuses according to concept of the "bolus watching" technique (correlation coefficient $r = 0.78$; $p < 0.005$). Average timing from readers and the measured steady state's delay were correlated ($r = 0.75$; $p < 0.005$), the mean delay from readers was shorter than the delay measured on time intensity curves but without a statistically significant difference (20.8 seconds versus 21.8 seconds; $p = 0.24$).

Conclusion

Steady state of contrast enhancement in brain parenchyma is required throughout acquisition time for correct FPCT CBV measurements. With clinically acceptable contrast agent volumes, steady state is a brief condition thus fast rotation speed acquisitions are needed. The use of central venous injections decreases the variability of steady state's delay from injection.

From this study it is possible to describe an examination protocol that does not require test injections anymore but that would not be suitable for all patients. "Bolus watching" technique is an interesting way to overcome inter-individual variability but may not always be the guarantee of steady state during whole acquisition.

Further studies are needed to optimize and standardize injections protocols to allow a larger diffusion of the FPCT CBV measurement during endovascular stroke therapy.

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