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Era?**

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Color-Coded Digital Subtraction Angiography: The End of a Monochromatic Era?

In 1927, Egaz Moniz^{1,2} introduced cerebral angiography by using the x-ray absorption of intravascular contrast. During the following 83 years, this way of studying the cerebral blood circulation has not significantly changed. In 2010, we still visualize the neurovascular system by injecting radiopaque contrast medium through a catheter that is directly placed into the carotid artery. Modern high-resolution neuroangiography provides superb visualization of the smallest vessels, acquired simultaneously in 2 projections, and allows very precise morphologic diagnosis of most cerebrovascular disorders. Although constantly improved during the decades, computerized and digitized vascular morphology is evaluated by using monochromatic displays.

Hence, the cardinal question raised by the article of Strother et al³ is whether neuroangiographers need to read a cerebral angiogram in color. Will it actually add relevant information when we colorize the blood flow velocity in cerebral arteries and visualize the arteriovenous malformation (AVM) feeder in red and the draining veins in blue? Or will it just produce other sorts of “pretty pictures” on our workstations?

Perceiving color allows humans to discriminate objects on the basis of the distribution of the wavelengths of light reflected to the eye. While differences in luminance are often sufficient to distinguish objects, color adds another perceptual dimension that is particularly useful when differences in luminance are subtle or nonexistent. Color gives us a different way of perceiving and describing the world we live in. The display of color can be used to enhance our perception of medical information derived from monochromatic CT, MR imaging, or sonograms. Because human eyes perceive color differentiation over a wide range, even the slightest change in signal intensity will be more easily distinguished with the naked eye.⁴

Attempts to use color in medical imaging go back to experiments in the 1980s involving x-ray exposures to the same objects by using different x-ray wavelengths.⁵ Color imaging has been introduced into clinical practice by developing sonographic scanners that allow separating arterial from venous blood by detecting different flow directions and encoding them with red and blue, respectively.⁶ Other evolving fields of color application are functional MR imaging and diffusion tensor imaging.

The increasing use of 3D datasets and sophisticated graphic workstations allow the ability to segment and render various anatomic structures in their natural colors. However, although these techniques are visually appealing and didactically very useful, most radiologists still prefer to rely on diagnosis with high-resolution monochromatic image data. This preference may change only when additional information becomes readily available.⁵ Besides functional MR imaging and color Doppler sonography, this reluctance to change

appears to be the case recently with positron-emission tomography/CT.

X-ray-based catheter angiography has, for a long time, been the dominant diagnostic tool for vascular lesions in the human body. Providing superior spatial resolution for vascular imaging that was continuously increased with time, conventional angiography has played a major role in diagnosing steno-occlusive diseases in cerebral, coronary, and peripheral vascular territories. After the introduction and rapid progress of cross-sectional imaging methods, such as CT angiography, MR angiography, and Doppler sonography in the late 80s and early 90s, many radiologists believed that these noninvasive methods would soon completely replace intra-arterial angiography. Mainly due to the inherent invasiveness and the potential risks of intra-arterial catheterization and contrast injections causing permanent neurologic deficits, those proponents of less “dangerous” vascular imaging loudly prophesied the near end of cerebral angiography as diagnostic tool. Twenty years later, intra-arterial digital subtraction angiography (DSA) not only still exists but also has become an indispensable imaging technique for endovascular treatment (EVT) methods that have largely replaced surgical techniques for vascular disorders. EVT plays a particularly important role in the modern management of neurovascular diseases.

Although it is a century-old technique, surprisingly the potential of serial conventional angiography appears still not fully explored. Emphasis over the years has been mainly on an increase of the contrast-to-noise ratio and spatial resolution or on the improved tolerance for contrast media. Compared with CT and MR imaging, relatively little research and development resources have been invested to further develop DSA technology.

3D rotational angiography (3D-DSA) was introduced in the late 90s, long after 3D CT and MR imaging data were in use on radiologic workstations. 3D-DSA, providing a new approach to complex vascular anatomy, has dramatically increased the safety and efficacy of neuroendovascular treatment and is today an integral part of neuroangiographic work-up. The development of cross-sectional imaging by using conebeam CT reconstructions represented another major step forward and has taken the imaging capabilities in the angiographic suite to a new level. It allows soft-tissue imaging to detect brain injuries during EVT,⁷ provides high-resolution imaging of small metallic implants,⁸ and helps in analyzing minute and complex vascular anatomy.⁹ Continuously increasing computing power and improving software will further revolutionize angiographic image postprocessing.

What is noteworthy, one major component of conventional angiography has been widely neglected in all these years: the inherent physiologic information of a serial angiogram that can capture the contrast propagation through blood vessels today with a rate of ≤ 30 frames per second. No other imaging technique, except for real-time Doppler sonography, provides such high temporal resolution. It is somewhat astonishing that though of interest early on,² this fundamental component of arteriography remained for so long more or less unused for diagnostic purposes. Besides subjective qualitative evaluations with rather imprecise distinctions into high- or low-flow conditions, functional information is usually not extracted from serial arteriograms. Cerebral circulation time,

used in the 70s to distinguish different forms of cerebrovascular flow compromise,^{5,10} is not part of neuroangiography practice today. More than 20 years ago, the first attempts to quantify angiography by using parametric color-coding were reported.^{11,12} Hunter et al, in 1986,¹² presented an interesting postprocessing technique to extract physiologic information by using time-attenuation curves. They were able to prove that such an approach can add useful information about renal, cardiac, and cerebral perfusion. Most curious, it was even demonstrated in 1 of the authors' cases that a left carotid occlusion may lead to a 3-second delay in perfusion of this hemisphere.

It is perplexing that this pioneering work has been widely neglected by both the scientific community and the medical imaging industry. Why so? Probably, because the use of color in medical imaging in general was still in its early stages and the era of computed digital imaging had just begun. Possibly also, because Hunter et al¹² were simply ahead of their time, a period in which most radiologists thought conventional angiography would soon disappear from the radiologic imaging armamentarium.

Applying color schemes to cerebral angiography is not trivial and may cause several problems. Inaccuracy of color scaling can become misleading, confuse readers, or even introduce errors. It has become increasingly easy in medical imaging to create powerful images that may trick the observer into taking them for reality.¹³ The use of time-attenuation methods, as initially suggested by Hunter et al,¹² may be less accurate because they produce only an estimate of the average velocity.¹³

Reproducibility of color-coding could be another issue requiring calibration techniques to ensure accuracy for pre- and postprocedure comparisons or for longitudinal studies. All injection parameters, such as the amount of contrast, duration of the injection, and catheter position in the carotid artery need to be kept constant. Cerebral circulation is further influenced by age and by metabolic factors such as the carbon dioxide concentration. The ability to control all possible confounding factors was beyond the scope of the preliminary experience presented here. Systematic validation of this technique by using an animal model and reference methods such as Doppler sonography is the next necessary step to further explore possible clinical applications. As stated by the Strother et al,³ another limitation of their study is possible selection bias in their material and the absence of values of normal flow conditions. It will be useful to study a group of healthy (in the sense that the circulatory system being studied is not affected) volunteers to establish baseline values. The collection of data in different groups of vascular diseases should help to gain valuable pathophysiologic insights.

It is not likely that color imaging in cerebral angiography will replace monochromatic imaging in the foreseeable future, but rather it may become an adjunctive tool for a more complete evaluation of the examination. Color imaging in cerebral angiography could serve as a validation and probably useful complementation of computational flow dynamic (CFD) studies, which will soon be available on our angiographic workstations.

Color-coded DSA in this article is not just an enhancement of the morphologic information in monochromatic DSA images. The use of a parametric color-coding may allow an easier

visual evaluation and quantification of the functionality of the blood circulation under normal conditions as well as under various pathologic circumstances.

Displaying the relative speed of the contrast passage through the cerebral circulation may facilitate recognition of under- and hyperperfused areas in the cerebral circulation. The calculated velocity data may be combined with a 3D data set of the same vascular tree that often is acquired during a neuroangiographic work-up. Using the cross-sectional area of the vessels, one can estimate the blood flow and blood volume.¹⁴ Such information could be used as a sort of "angiographic perfusion" study and may develop into an interesting tool to assess and differentiate complex restrictions of blood supply to the brain (eg, due to steal, steno-occlusive diseases like vasculitis and Moyamoya syndrome, or reactive vasospasm). This approach seems even more appealing because it comes with no additional radiation dose, currently a major concern for CT perfusion for the evaluation of patients with stroke.¹⁵

Parametric color schemes are widely applied today in CFD studies, a new technique that is recently gaining popularity for improving our understanding of cerebral hemodynamics.¹⁶ If a standard diagnostic angiogram will allow a similar evaluation of the physical forces inherent to normal and pathologic blood flow, the immediately available physiologic information could reach significant importance. Apart from faster identification of a rapidly shunting AVM compartment due to an intranidal direct fistula, numerous other clinical applications can be envisioned. These could include the study of intraneurysmal hemodynamics by using patient-specific flow data and tailored flow-diverting devices. Effects of endovascular recanalization procedures such as intracranial angioplasty and stent placement could become assessable in a more objective comparable manner.

Finally, the often-criticized invasive nature of cerebral angiography simply demands the use of all information available. Thus, it is my sincere hope that neuroangiographers do not have to wait another 20 years until industry picks up on this (old and new) concept and provides us with user-friendly software and powerful hardware, not just to create visually appealing images but to gain useful physiologic information that will enhance our diagnostic capabilities and improve outcome in patients undergoing EVT. The authors are to be congratulated in their attempt to push angiographic technology toward something that may someday be called "functional angiography."¹⁷

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