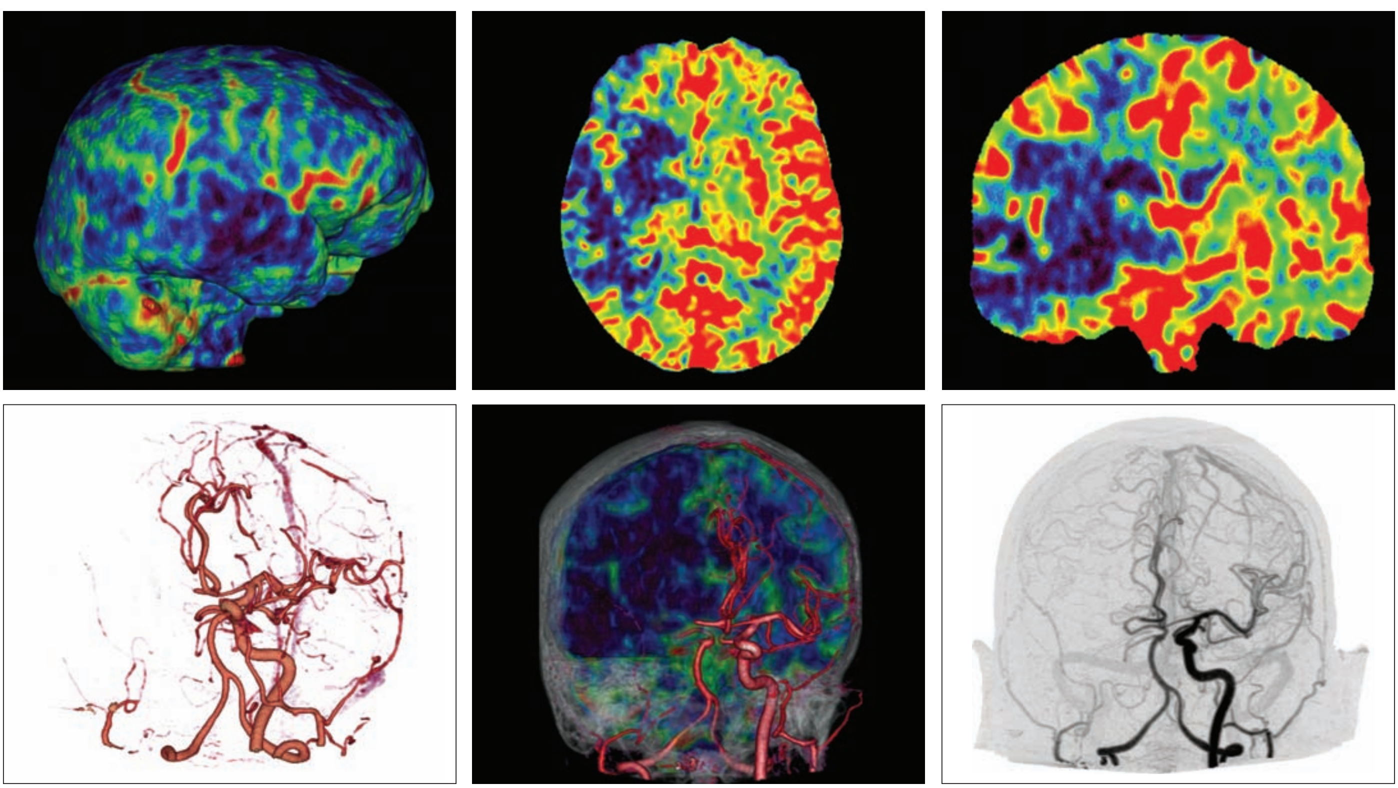
Leading Innovation

Neuro and Acute Stroke Imaging with Dynamic Volume CT

Richard Mather, PhD

Senior Manager, Clinical Science
Toshiba America Medical Systems, Inc.



Stroke, the sudden loss of blood flow to part of the brain, is both the third leading cause of death[1] and the leading cause of serious long-term disability[2] in the United States. It is estimated that, in 2008, the total direct and indirect costs associated with stroke in the US will be $65.5 billion[3]. A stroke patient's prognosis is heavily determined by the speed with which blood flow can be restored to the distressed region of the brain: approximately 1.9 million neurons are lost every minute during a stroke[4]. The sooner blood flow can be restored to the afflicted portion of the brain, the better the patient's outcome, leading to the maxim "time is brain". Once the patient is brought in for emergency care, diagnostic imaging plays a critical role in the evaluation and management of the patient. In a suspected stroke case, conventional evaluation entails multiple CT exams. However, since conventional CT is constrained to imaging only a limited portion of the brain, an MR study is often also called for to assess the entire brain. All together, these imaging exams can definitively determine the location and extent of the stroke as well as the amount of brain tissue that might be saved by returning blood flow to the affected area of the brain. However, in a situation where every second counts, these multi-modality exams take a significant amount of time. The Aquilion ONE dynamic volume CT scanner, on the other hand, can complete whole brain stroke characterization in minutes.

In current emergency care practice, a battery of imaging exams is necessary to assess a patient for acute stroke. When all these diagnostic imaging options are available at a given facility, and when an individual patient is not contra-indicated for MR, the results can be very sensitive in defining the severity and extent of the stroke. However, most centers do not have 24/7 MR service and many patients have medical conditions such as aneurysm clips and pacemakers that preclude an MR exam. Furthermore, it can take several hours to complete all the tests, and every minute that goes by can make the difference in the survival and subsequent quality of life of a stroke patient.

Toshiba's Aquilion ONE offers complete stroke characterization in only minutes and with a single imaging exam. The Aquilion ONE is a 320 detector row dynamic volume CT scanner that allows for the coverage of up to 16 cm of anatomy per gantry rotation. Therefore, many organs, including the entire brain, can be imaged with a single rotation and without table motion. This unique ability makes dynamic imaging of an anatomical volume simple and robust. When contrast material is flowing through the anatomy, the Aquilion ONE captures the entire brain at a single moment in time, acquiring temporally-uniform volumes either continuously or at discrete time points to create a unique and powerful dynamic volume dataset.

Since this dynamic volume dataset contains both anatomic and functional information, it can be rapidly analyzed to deliver comprehensive information for the evaluation of acute stroke.

STROKE AND STROKE TYPES

In the United States someone suffers from a stroke every 40 seconds[3]. The short term and long term prognoses of a stroke patient are heavily dependent on several disparate factors including the location of the stroke, the extent or size of the ischemia, the magnitude of the flow reduction to the affected parenchyma, the individual autoregulation at work in the patient, and the duration of time from the onset of the ischemia until flow is restored.

Strokes fall into two distinct categories: hemorrhagic and ischemic. Hemorrhagic strokes occur when there is bleeding either inside the brain, or in the subarachnoid space between the brain and the skull. In either case, there is an excess of pressure exerted on the brain causing damage to the brain cells. While hemorrhagic stroke has a lower survival rate, it is also significantly less common, accounting for only about 17% of all strokes.

Ischemic strokes, on the other hand, occur when an artery supplying the brain is blocked. There are two primary ways that this blockage can occur. The more common way, occurring in about 50% of all stroke patients, is when cholesterol builds on the inside of the vessel causing it to narrow. When the vessel gets too narrow, the blood starts to collect and form a clot, or thrombus, which can, in some cases, completely obstruct the flow of blood in that artery. Therefore, this type of stroke is called a thrombotic stroke (Figure 1). In about 30% of all strokes, a blood clot is formed somewhere else in the body and becomes dislodged. This "thrown clot" travels through the vascular system until it gets lodged in a vessel that is too small to let it pass, obstructing that vessel's flow. If this vessel is in the lungs, the result is a pulmonary embolism. On the other hand, if this vessel is in the brain, it becomes an embolic stroke (Figure 2).

THE ROLE OF IMAGING IN STROKE

Whatever the cause of the stroke, imaging plays a critical role in the management of the patient. The first question that needs to be answered is whether the patient has suffered a hemorrhagic or ischemic stroke, since the treatment pathways are very different for each of these possibilities. The best way to answer this question quickly is to perform a non-contrast enhanced CT scan of the head. Any area of hemorrhage or "bleed" can be clearly depicted by changes in the CT density of the brain (Figure 3). If the bleed is acute and has occurred within about 4 hours, the blood will show up as an area of increased attenuation and will often have a surrounding area of low attenuation, representing edema[5].

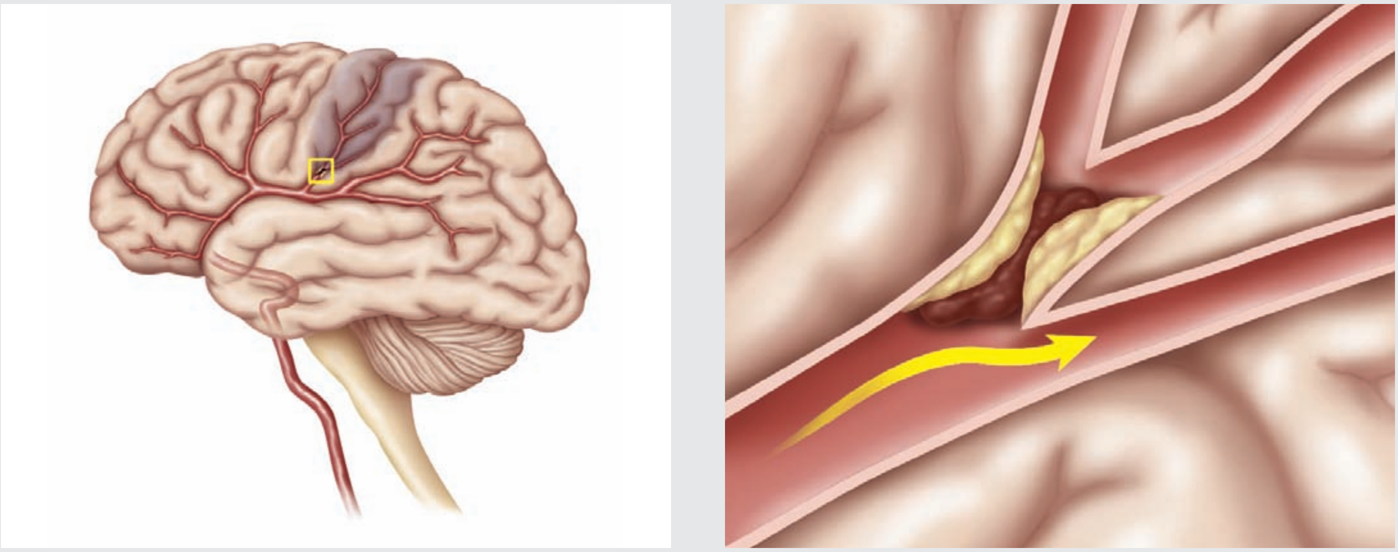


Figure 1: Thrombotic stroke: As the arteries become narrow from atherosclerosis, the likelihood increases that the turbulent flow within the small lumen may cause a clot, or thrombus to form. This clot can occlude the entire vessel and deny blood supply to the tissue beyond the blockage.

If no bleed is seen, the next step is to determine if there are any blockages in the neurovascular structure. This assessment is done via a CT perfusion scan and a contrast enhanced CT angiogram (CTA) of the head. Figure 4 shows a subtracted CT angiogram of a patient with a severe left MCA stenosis. By identifying the location and extent of the blockage, the appropriate treatment plan can be formulated.

PERFUSION, INFARCT, AND PENUMBRA

Once the non-contrast CT has ruled out the existence of a hemorrhage, the most important role of imaging in acute stroke assessment is to measure the perfusion in every part of the brain to determine those areas that are beyond repair and more importantly, those areas that can be saved through intervention. When the blood supply is suddenly lost, a portion of the brain dies quickly and forms what is known as the infarcted core. There is, however, another region of affected tissue that is receiving some blood from collateral flow. The brain cells in this region do not die as rapidly as those in the infarcted core and may live for a few hours or even for a few days. This region is known as the ischemic penumbra or simply penumbra (Figure 5). As time without oxygen goes on, the tissue in the penumbra dies and the infarcted core expands. Eventually, the entire penumbra will become infarcted if the blood flow is not restored. The main goal of ischemic stroke treatment is to rescue the tissue in the penumbra by returning blood flow to that region.

The current standard of practice in acute stroke therapy is to assume that beyond a fixed time window of 3 hours, thrombolytic (or clot-busting) therapy will not be effective. While the amount of salvageable penumbra is certainly a function of the time passed since the stroke occurred, with nearly all patients having ischemic penumbra for up to 3 hours after the loss of flow, it is also heavily dependent on the patient's own physiology. Some reports have shown that a significant majority of patients have surviving penumbra even at 6 hours[6,7,8]. However, trials looking at patient outcomes with thrombolytic therapy between 3 and 6 hours after the stroke have shown relatively

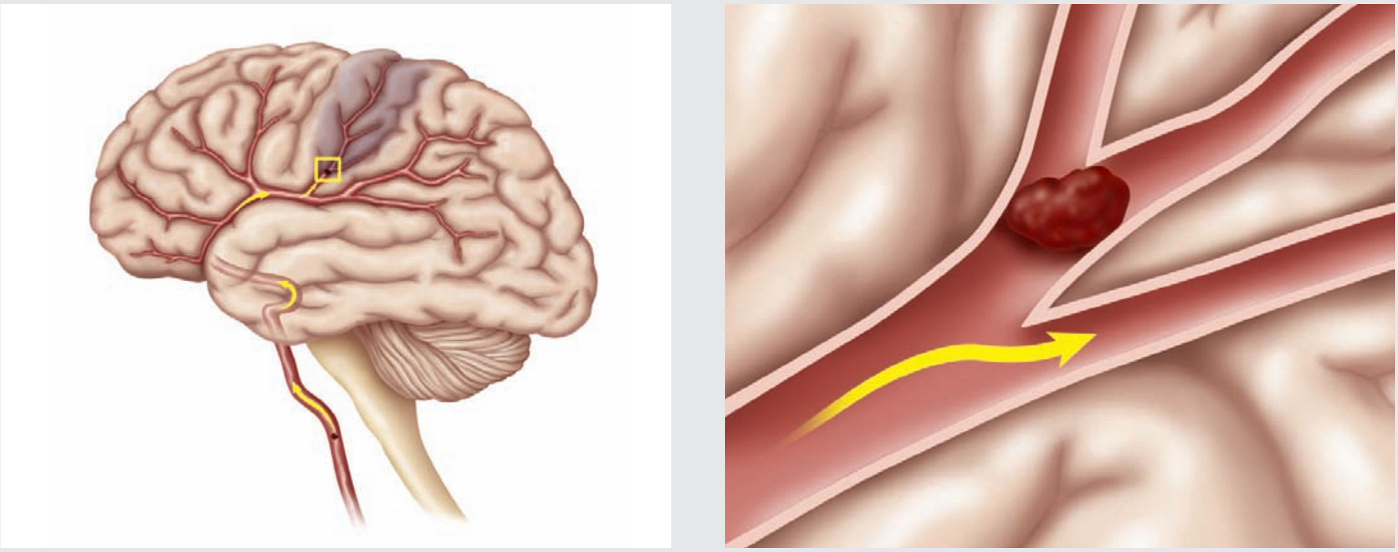


Figure 2: Embolic stroke: Sometimes, pieces of atherosclerotic plaque can break free and travel to the brain through the blood vessels. These emboli or "thrown clots" can get lodged within a vessel in the brain and block the supply to a portion of the brain.

negative results so far[9]. These results are likely due to the fact that the trials did not use imaging to select patients for therapy based on the existence of ischemic penumbra[10]. If the patients that still have penumbra beyond 3 hours can be positively identified, the window for thrombolytic therapy could be based on individual patient physiology and extended, rather than adherence to a rigid time rule. In order to improve patient outcomes with extended therapy, it is necessary to accurately and rapidly measure the presence and extent of ischemic penumbra in each individual patient[11,12].

PENUMBRA IMAGING IN THE BRAIN

While there are several imaging modalities that can measure perfusion in the brain, there are two that are most useful in defining areas of infarct and the penumbra region: CT and MR. Both modalities have specific strengths and weaknesses in their abilities to image penumbra. The performance of an imaging modality is based on its availability to stroke patients, its sensitivity to differentiating between infarct and penumbra, its spatial resolution to accurately define the extent of the infarct and penumbric regions, and the speed with which the exam can be carried out.

MR imaging is very sensitive to small differences in soft tissue. For the evaluation of penumbra, a combination of two different imaging sequences is needed. Diffusion weighted imaging (DWI) is sensitive to the Brownian motion of the water molecules within the brain. On a DWI MR exam, the visible lesion corresponds to the infarcted core of the stroke. However, perfusion weighted MR shows the entire area of decreased perfusion and the difference between these areas corresponds to the ischemic penumbra. MR also has the added benefit of not using ionizing radiation. On the other hand, MR imaging in acute stroke has several drawbacks as well. Especially for stroke, when minutes matter, the exam takes a relatively long time, approximately 30 minutes for a highly streamlined stroke protocol. Furthermore, there is a relatively limited availability of 24/7 MR scanners in an emergency setting. Finally, since it is often difficult to get a complete patient

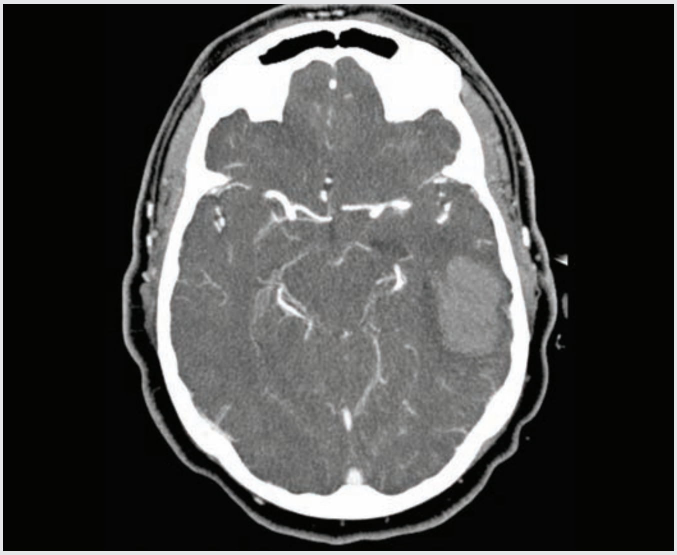


Figure 3: Intracranial hemorrhage: The acute bleed in this patient is shown as an area of increased attenuation in the left hemisphere. The area of low attenuation surrounding the hemorrhage is the associated edema.

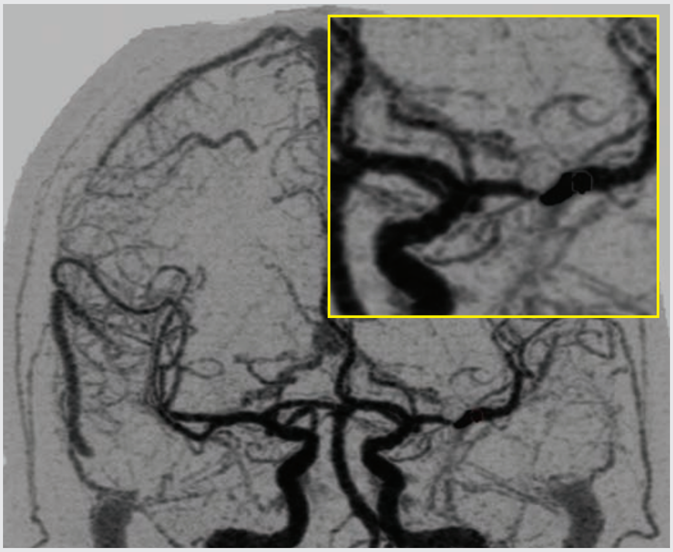


Figure 4: The inset shows a magnified view of the severely stenosed section of the left MCA.

history in an emergency setting and rule out contraindications such as aneurysm clips, the use of MR in acute cases can be limited.

CT imaging, however, has distinct advantages in speed and around-the-clock availability. Since the first imaging exam, even if an MR is available, is usually a non-contrast CT scan, the patient is already at the CT scanner and ready for CT perfusion imaging. Furthermore, there are fewer contraindications to CT scanning and no renal failures have been reported following a perfusion CT exam[13]. The most significant limitation to perfusion CT in acute stroke imaging to date has been its limited craniocaudal coverage. Since available multidetector CT (MDCT) scanners can only image 3-4 cm in a rotation, MDCT cannot evaluate perfusion over the entire brain.

THE NEED FOR WHOLE BRAIN CT PERFUSION IMAGING

There has been some discussion about ways to modify MDCT scanners to increase their limited coverage for perfusion imaging. With a scanner that acquires less than the entire head in a rotation, the clinician has to make some sacrifices in either coverage or accuracy (Figure 6). While the limited coverage, dynamic perfusion available with MDCT systems gives precise perfusion calculations in the 3-4 cm covered, this type of scan cannot visualize large portions of the brain. A trade off approach is to rapidly move the patient back and forth through the gantry to cover larger areas of the head. While this method can give the appearance of acquiring multiple volumes over time, each individual volume is actually not temporally uniform: the beginning of the volume is imaged several seconds earlier than the end of the volume. Furthermore, since the scans take place in both directions, the temporal sampling is non-uniform as the edges of the volume are imaged twice quickly and then not again for a long time. Since perfusion algorithms are dependent on the time of contrast flow through the tissue in relation to the input blood flow from the supply artery and the output blood flow from the draining vein, this temporal non-uniformity results in blurred and inaccurate perfusion values over the volume. Also, with repeated helical

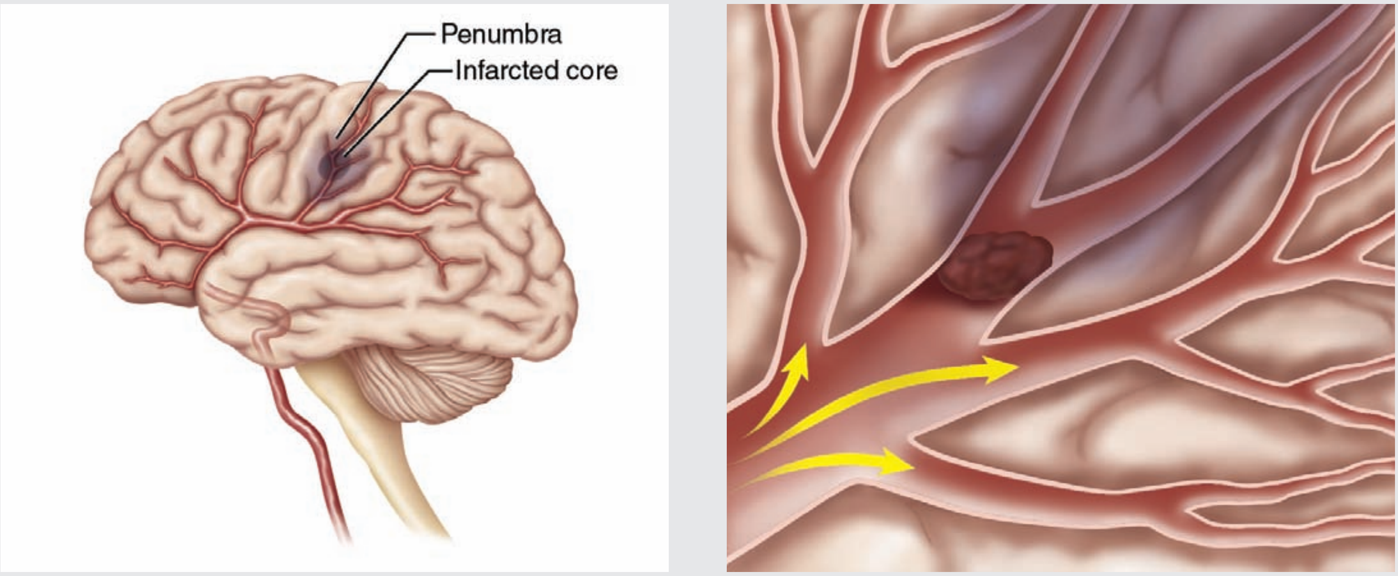


Figure 5: Ischemic penumbra: When a stroke occurs, a portion of the affected area, known as the infarcted core, is left with critically low blood supply and dies quickly. However, surrounding that area is a region where the blood supply is reduced, but less critically and the brain tissue can survive for a time. This area, called the ischemic penumbra, can be saved and is the target for stroke intervention.

scanning comes a substantial increase in x-ray dose due to the overlapping pitch and over-ranging.

While this kind of approach increases the coverage of the volumes, it can never accurately capture the entire volume at a distinct time point. Furthermore, it cannot accurately visualize the dynamic flow of contrast through the entire volume or evaluate the timing of contrast arrival in different parts of the neurovascular structure. The only way to get accurate whole brain perfusion and temporally uniform dynamic blood flow information about blood in the neurovasculature is to have sufficient anatomic coverage with the detector to image the entire brain in a single rotation (Figure 7).

MULTIDETECTOR CT STROKE IMAGING

A typical streamlined stroke protocol using a conventional, multidetector CT machine (16, 64, or 128 multidetector row) starts with a non-contrast enhanced exam of the head. This is a relatively low dose helical exam that takes six to ten seconds to perform and delivers approximately 3 mSv of radiation dose. At this point, the clinician examines the image data to determine whether a hemorrhage is present. This takes about 5 minutes for reconstruction and review. If there is a hemorrhage, the patient goes immediately to intervention to control the bleeding; otherwise, a limited coverage CT perfusion exam is performed. This exam takes about 60 seconds as the scanner intermittently monitors the passage of contrast material through the 3-4 cm of parenchyma around the Circle of Willis. It delivers approximately 2-3 mSv of radiation dose and uses 50 ml of iodinated contrast material. Finally, a helically acquired, single phase CTA is performed capturing the arterial flow. This exam uses another 50 ml of contrast material and an additional 1.5-2 mSv of radiation dose. The entire process, including patient preparation, takes about 10 minutes and can rule out an intracranial bleed, can visualize a single, static phase of blood flow, and evaluate the perfusion in part of the brain. However, the perfusion portion is limited by its coverage, so an MR perfusion/diffusion exam is often required to evaluate the penumbra in the rest of the brain[14].

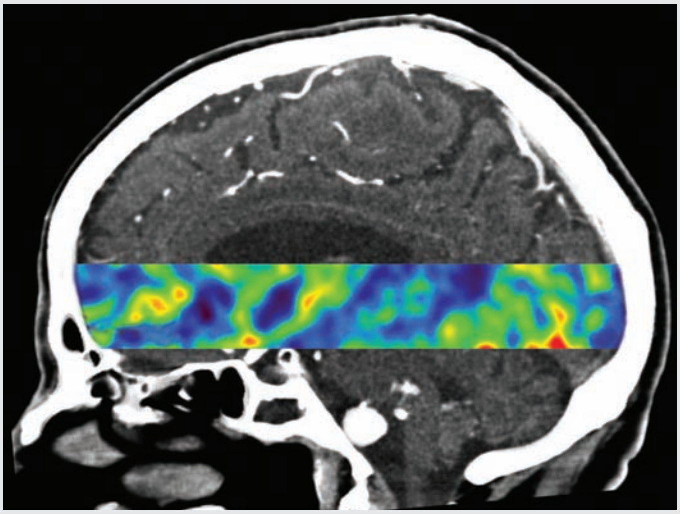


Figure 6: MDCT perfusion scanning: With a scanner that acquires less than the entire head in a rotation, the user has to make some sacrifices in either coverage or accuracy. This image shows accurate perfusion values over the narrow range that can be imaged dynamically without table motion using a conventional multidetector system.

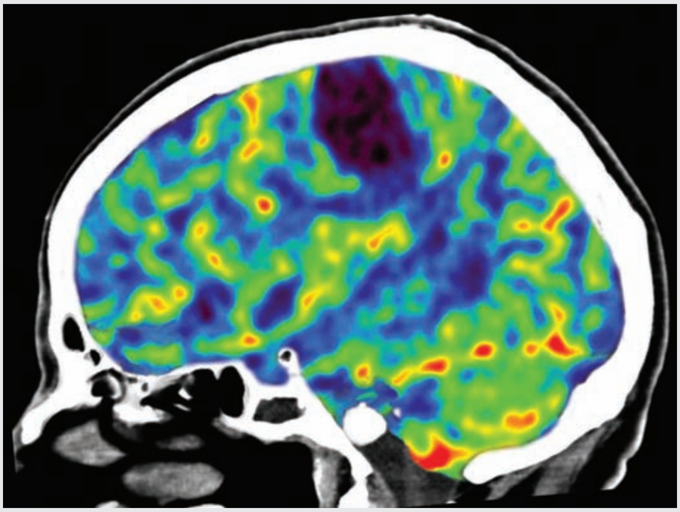


Figure 7: Dynamic volume perfusion scanning: With whole head volumetric coverage, the Aquilion ONE acquires accurate perfusion maps of the entire brain showing the large, superior lesion that would have been completely missed using MDCT technology.

AQUILION ONE STROKE IMAGING

The dynamic volume capabilities of the Aquilion ONE scanner, on the other hand, are uniquely positioned to revolutionize the diagnosis and evaluation of acute stroke. With a single axial rotation, the non-contrast examination of the brain can be performed in 1 second. If no hemorrhage is found, a single injection of contrast material is administered and the entire brain is imaged intermittently over about 60 seconds. From this single exam of less than one minute, the data can be analyzed to look at any individual arterial or venous phase, to look at dynamic subtraction angiography with full flow information, and to look at whole brain volumetric perfusion. The total exam uses less than 5–6 mSv of radiation dose, about 50 ml of iodinated contrast, and can be completed in less time than even the most streamlined 64 or 128 detector protocol. Furthermore, with whole brain perfusion and dynamic angiography, the Aquilion ONE gathers all the information the clinician needs to evaluate the penumbra in the entire brain.

CONCLUSION

With 1.9 million neurons being lost each minute in an acute stroke[4], every second counts. The faster the clinician can determine the optimal treatment pathway, the better the patient's chances for survival and recovery. With its ability to image the entire brain in one rotation, the Aquilion ONE is uniquely suited to rapid whole brain perfusion imaging. All necessary information to diagnose and evaluate acute stroke can be acquired with one examination on one scanner with one injection of contrast. The Aquilion ONE offers comprehensive diagnostic information in less time with lower doses of both radiation and contrast material.

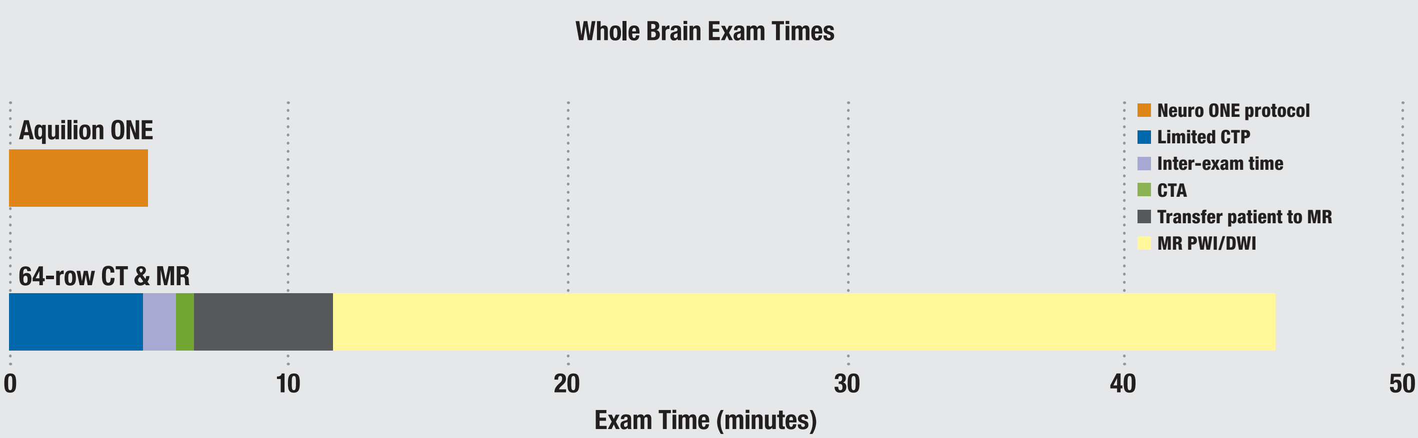


Figure 8: Whole brain perfusion exam times. This graph compares the time required to assess the vascular anatomy and perfusion in the entire brain using the Aquilion ONE versus using a 64-detector row CT supplemented with MR perfusion and diffusion weighted imaging for whole brain coverage. The Aquilion ONE acquires all the data necessary and displays it in less than 7 minutes. A 64-detector row CT acquires a separate CTA exam (with a separate injection of contrast material) and only acquires limited perfusion coverage. Therefore, in order to achieve whole brain coverage, an MR perfusion and diffusion scan are necessary.

Case Study: Perfusion Deficit

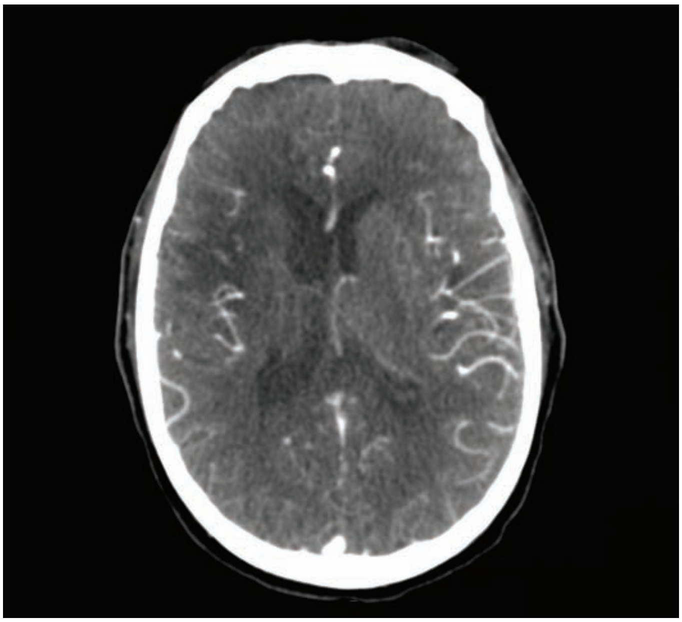
CLINICAL HISTORY

Patient presented with headaches, confusion and altered mental status.

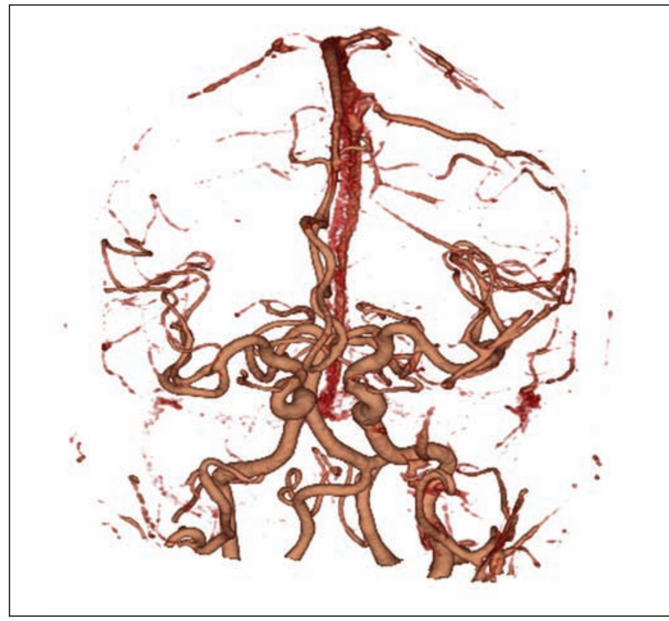
The Neuro ONE protocol was used to scan this patient. With this protocol, the Aquilion ONE acquires 19 volumes of data intermittently for a total of 50 seconds to see the wash in and wash out of the contrast material. Initially, the scans are spaced every other second for a good representation of the upslope and peak opacification. Toward the end, in the wash out phase, the scans are spaced wider to save radiation dose. These dynamic volume scans are acquired using all 320 detector rows, each measuring 0.5 mm. The analysis software provides a clinical result in less than 5 minutes from the start of scanning.

This scan protocol provides the physician with a comprehensive dataset for assessing anatomy, flow, and perfusion of the entire brain. Since it contains true 4D information (isotropic 3D volumes over time), all the static, dynamic, and functional reconstructions can be viewed and sculpted in any orientation. From this single acquisition of data, the user can evaluate the data in multiple ways. It can be viewed as a CTA exam showing pure arterial opacification, pure venous opacification, or any phase in between. These phases can be separately rendered and then fused for a single display of the arteries and veins. Alternately, the dataset can be viewed in 4D dynamic flow which is a CT dynamic subtraction angiogram. This data can be rotated and sculpted to view the dynamic flow in a portion of the brain and in any arbitrary orientation. Finally, the dataset can be analyzed for whole brain perfusion with maps showing regional cerebral blood volume (rCBV), regional cerebral blood flow (rCBF), mean transit time (MTT), time to peak, and a delay map that highlights mismatches in arrival time. These maps can be used to visually and quantitatively assess decreased perfusion to any part of the brain.

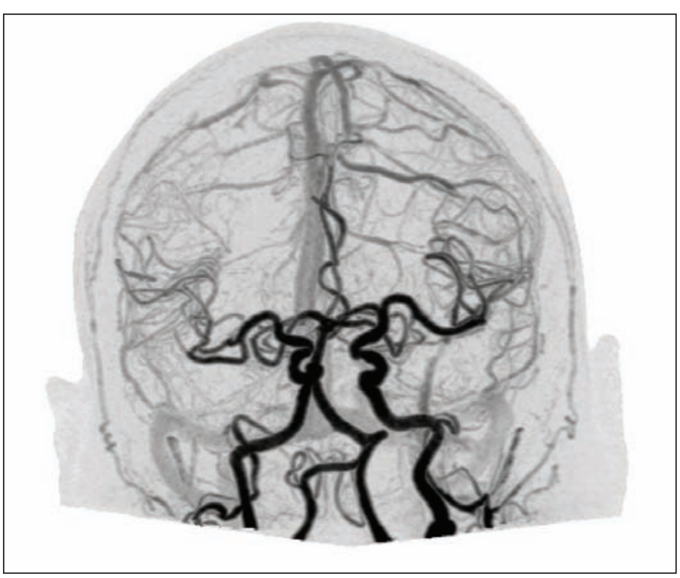
This patient shows an infarcted region that is seen as an area of low density in the post-contrast scan. Analysis of the dynamic volume rendered and dynamic inverted MIP reconstructions reveals a marked lack of flow on the right side and a mild stenosis in the M2 segment of the right middle cerebral artery. Additionally, the perfusion maps reveal a decreased flow and volume on the right side consistent with the infarcted region seen in the post-contrast image. Furthermore, the parenchyma in the territory of the MCA is at risk for ischemic disease. With a single injection of contrast and a single dynamic acquisition, the Aquilion ONE captures all the information necessary to evaluate this patient.



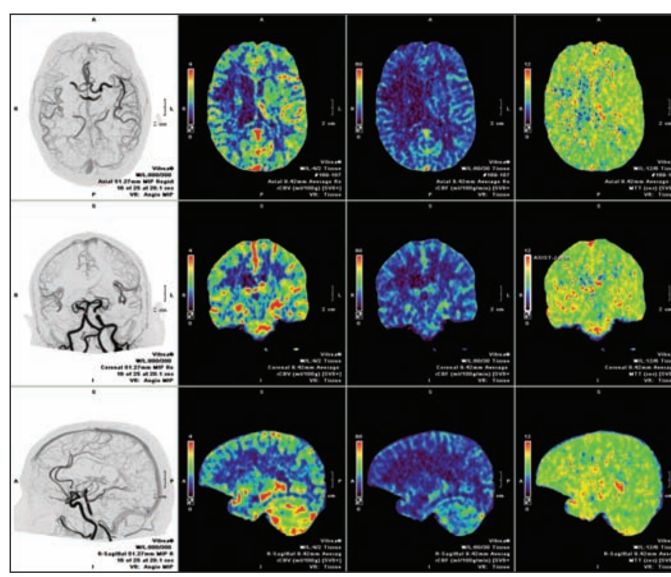
Post contrast axial brain. This axial image shows an infarcted area in the right hemisphere depicted as an area of low density and decreased vessel enhancement following contrast infusion.



3D volume rendered CTA. This volume rendered view in the arterial phase shows the craniocaudal coverage of the Aquilion ONE capturing the arteries in the entire brain. While this static view shows a decrease in flow on the right side, the flow information is better appreciated in dynamic mode and can be seen at: **www.dynamicvolumeCT.com**



3D inverted maximum intensity projection CTA. This view is during the late arterial phase and is shown in the coronal plane. It clearly shows the relative lack of vascular flow on the right side as well as a mild stenosis in the M2 segment of the right middle cerebral artery. The dynamic representation of this 4D CT DSA can be seen at: **www.dynamicvolumeCT.com**



Perfusion maps and angiographic views. These perfusion maps with their corresponding angiographic views show a marked decrease in rCBF and rCBV on the right side. These correspond to the decreased blood flow in the MCA distribution territory on that side and this tissue is at risk for ischemic disease.

References:

1. *NCHS mortality data. Available online: http://www.cdc.gov/nchs/data/nvsr/nvsr56/nvsr56_05.pdf*

2. *SIPP; MMWR Morb Mortal Wkly Rep. 2001;50:120–125.*

3. *http://www.americanheart.org/downloadable/heart/1200078608862HS_Stats%202008.final.pdf*

4. *Saver JL.. 2005, Time is Brain - Quantified. Stroke 37:263-266.*

5. *http://www.emedicine.com/RADIO/topic99.htm*

6. *Hossmann KA. 1983, Neuronal survival and revival during and after cerebral ischemia. Am J Emerg Med 1:191–197.*

7. *Hossmann KA. 1994, Viability thresholds and the penumbra of focal ischemia. Ann Neurol 36:557–565.*

8. *Read SJ, Hirano T, Abbott DF, et al. 2000, The fate of hypoxic tissue on 18F-fluoromisonidazole positron emission tomography after ischemic stroke. Ann Neurol 48:228-235.*

9. *Hacke W, Donnan G, Fieschi C, et al. ATLANTIS Trials Investigators; CASS Trials Investigators; NINDS rt-PA Study Group Investigators. 2004, Association of outcome with early stroke treatment: pooled analysis of ATLANTIS, ECASS, and NINDS rt-PA stroke trials. Lancet 363:768-774.*

10. *Wintermark, M. 2005, Brain perfusion-CT in acute stroke patients. Eur Radiol: 15[Suppl 4]: D28-D31.*

11. *Kaste M. 2004, Reborn workhorse, CT, pulls the wagon toward thrombolysis beyond 3 hours. Stroke 35:357–359.*

12. *Donnan GA, Davis SM. 2002, Neuroimaging, the ischaemic penumbra, and selection of patients for acute stroke therapy. Lancet Neurol 1:417–425.*

13. *Smith WS, Roberts HC, Chuang NA, et al. 2003, Safety and feasibility of a CT protocol for acute stroke: combined CT, CT angiography, and CT perfusion imaging in 53 consecutive patients. AJNR 24:688-690.*

14. *Tomandl BF, Klotz E, Handschu R,et al. 2003, Comprehensive imaging of ischemic stroke with multisection CT. Radiographics 23:565–592.*

Made for Life

TOSHIBA AMERICA MEDICAL SYSTEMS, INC.

2441 Michelle Drive, Tustin CA 92780 / 800.421.1968

CTWP1068US