Intracerebral hemorrhage (ICH) is described as spontaneous extravasation of blood into the brain parenchyma. This clinical entity is present in 10% to 15% of all stroke cases in the Western population, with reported incidence rates higher in Asia. It is also associated with a higher mortality rate compared with either ischemic stroke (IS) or subarachnoid hemorrhage.

ICH is classified according to its primary (80% to 85%) or secondary (15% to 20%) causes. More than 50% of primary ICH events are directly correlated with hypertension as a risk factor, whereas ≈30% are known to be associated with cerebral amyloid angiopathy (CAA). The causes of secondary ICH include hemorrhage conversion of IS, amyloid angiopathy, stimulant drugs, vascular malformations (aneurysms, arterovenous malformations, venous angioma, cavernoma, dural arteriovenous fistula), coagulopathy (hemidacrytary, acquired, induced by anticoagulants or antiplatelets), neoplasms, trauma, vasculitis, Moyamoya disease, or sinus venous thrombosis.

Currently, ICH is classified as either primary or secondary according to only causes. However, this classification does not take into account the inherent differences of underlying vascular pathologies. Hence, a more systematic stratification based on new criteria is currently being developed. Specifically, Meretoja et al have proposed the SMASH-U classification, based on the underlying diseases of ICH: Structural lesions (cavernomas and arterovenous malformations), Medication (anticoagulation), Amyloid angiopathy, Systemic diseases (liver cirrhosis, thrombocytopenia, and various rare conditions), Hypertension, and Undetermined causes. This classification has proven to be feasible and is also associated with survival prognosis. Another classification used in clinical practice distinguishes between deep and lobar ICHs according to location. Deep ICHs are located in the basal ganglia, thalamus, internal capsule, cerebellum, or brain stem and are generally related to hypertension. Whereas, lobar ICHs usually require more extensive diagnostic testing because of their wider range of causes.

Regarding clinical outcome, ICH is commonly characterized by hematoma expansion and early neurological deterioration within the first few hours of onset. Thus, rapid management including diagnostic work-up needs to be performed.

We reviewed the available neuroimaging tools for ICH, as well as the changes in ICH in response to blood breakdown products, seen on CT and MR at various stages (Table 2). Both catheter angiogram and CT angiography (CTA) methods were also analyzed and compared for their advantages in different clinical situations. The purpose of our neuroimaging review of ICH was to provide a framework for choosing a rational diagnostic imaging plan, taking into account the clinical characteristics of the presenting patients. Because of the fact that a myriad of imaging modalities is available, it is important to understand the indications and limitations of each technique in order to select the most appropriate study for each patient.

Computed Tomography

Contemporary CT, including noncontrast CT (NCCT), perfusion CT, and CTA, is generally used for hyperacute stroke imaging. In fact, NCCT is commonly used in an emergency room setting for acute stroke because of its convenience and its high sensitivity for detecting ICH, which is a contraindication to thrombolytic therapy. Moreover, NCCT allows to quantify hematoma volume and monitor hemorrhage evolution in ICH accurately. That is, ICH volume can be calculated by using the ABC/2 method, derived from an approximation, according to the formula for ellipsoids, where A is the greatest hemorrhage diameter; B, the diameter at 90° to A; and C, the approximate number of CT slices with hemorrhage multiplied by slice thicknesses (Figure 1). Nonetheless, some studies assessing the reliability of the ABC/2 method have shown that it produces a larger percentage of error compared with other measurement techniques, particularly for irregular-shaped objects. In fact, comparing the ABC/2 method with the manual planimetric method, the former consistently overestimated infarct volume by a median false increase of 7.33 cm³. Whereas, the Quantom method for quantitative tomography has been reported to more reliably detect smaller changes in ICH volume compared with the ABC/2 method. This is because Quantom method measures the geometry of individual hematoma volumes, whereas the ABC/2 method approximates all hematoma volumes such as ellipsoid. To this regard, Huttner et al reported an overestimation of 32.1% in hematoma volume calculations for irregular and dichotomized shapes of hematomas among ICH patients with a history of warfarin use. Both initial hematoma volume and hematoma growth are independent predictors of clinical outcome and mortality. To date, though the ABC/2 method is the most readily available assessment at bedside, protocols for accurate assessment of hematoma volume...
whereas bone is between 700 and 3000.18,19 At onset, hematoma is between 37 and 45, white substance is between 20 and 30, water is equal to 0, blood is between 30 and 45, gray substance the attenuation coefficient of water. The Houndsfield units for units, according to the value of x-ray attenuation corrected for able to determine the approximate age of hematomas, by eval-

Table 1. Intracerebral Hemorrhage (ICH) Classification According to Causes

<table>
<thead>
<tr>
<th>Primary Causes</th>
<th>Secondary Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>Hemorrhage conversion of ischemic stroke</td>
</tr>
<tr>
<td>Cerebral amyloid angiopathy</td>
<td>Stimulant drugs</td>
</tr>
<tr>
<td>Vascular malformation</td>
<td></td>
</tr>
<tr>
<td>Aneurysms</td>
<td></td>
</tr>
<tr>
<td>Venous angioma</td>
<td></td>
</tr>
<tr>
<td>Cavernoma</td>
<td></td>
</tr>
<tr>
<td>Dural arterovenous fistula</td>
<td>Coagulopathy</td>
</tr>
<tr>
<td>Hereditary</td>
<td></td>
</tr>
<tr>
<td>Acquired</td>
<td></td>
</tr>
<tr>
<td>Iatrogenic (anticoagulants, antiplatelets)</td>
<td>Neoplasms</td>
</tr>
<tr>
<td>Trauma</td>
<td></td>
</tr>
<tr>
<td>Vascularitis</td>
<td></td>
</tr>
<tr>
<td>Moyamoya disease</td>
<td></td>
</tr>
<tr>
<td>Sinus venous thrombosis</td>
<td></td>
</tr>
</tbody>
</table>

and its characteristics should be incorporated into the CT scanner consoles, because this can allow the operator to obtain such information accurately in a timely manner.14 CT scan is also able to determine the approximate age of hematomas, by evaluating for the density of the lesions measured in Hounsfield units, according to the value of x-ray attenuation corrected for the attenuation coefficient of water. The Hounsfield units for water is equal to 0, blood is between 30 and 45, gray substance is between 37 and 45, white substance is between 20 and 30, whereas bone is between 700 and 3000.18,19 At onset, hematoma is commonly seen as uniform and smooth hyperintense signals on CT. Over the course of the first 48 hours, large hematomas tend to show fluid levels, indicating that they are not solidified yet.20 To this regard, fluid blood levels have been defined as a horizontal interface between hypodense bloody serum layerd above hyperdense settled blood. Fluid blood levels in acute ICH are moderately sensitive (59%) to the presence of coagulopathy (ie, abnormal prothrombin time and partial thromboplastin time) and highly specific (98%) for this condition.21 Blood/fluid levels are also frequent in thrombolysis-related ICH and associated with higher hemorrhage volumes.22 Over the first 72 hours, a hypodense region can be detected around lesions, as a result of the edema that surrounds the brain tissue; a noteworthy mass effect can be detected as well. Three to 20 days after onset, the lesion area tends to shrink and become less intense, losing ≥1.5 Houndsfield units per day. The periphery of the lesion tends to take on an uneven profile, which acquires a pseudoab-ssess (ring-like) appearance, as seen on contrast. Reductions in edema and mass effect can also occur up until the ninth week, when only a confined region of modest hypodensity can be observed on CT.23

Contrast-enhanced CTA is able to identify patients at high risk of hemorrhage enlargement (HE), by revealing a spot sign, which is a contrast medium extravasation within the hematoma.24 Spot sign is highly predictive of HE and has been reported to have a positive predictive value of 73%, a negative predictive value of 84%, sensitivity of 63%, and specificity of 90%.25 HE usually occurs in 30% of patients with ICH <3 hours of symptom onset,26 and the frequency of spot sign is highest in patients presenting <3 hours, but its accuracy in predicting HE remains high, regardless of time from symptom onset.27 Furthermore, spot sign is associated with poor prognosis, high rates of early clinical deterioration, high mortality, more severe clinical presentation, and decompression of the hemorrhage into the intraventricular space.25,28–33 ICH volume ≥30 cm³ together with Glasgow Coma Scale score, presence of intraventricular blood, and age ≥80 years have been included as independent variables for 30-day mortality in the ICH score developed by Hemphill et al.34 The utility of detecting the spot sign on clinical decision making and outcome improvement remains question-able. So, patients with spot sign are amenable to other studies,35 with the purpose of demonstrating the feasibility of CTA in the hyperacute phase and the reliability of spot sign in emergency setting for guiding the therapy with factor VII or other prothrombotic to avoid HE and, therefore, a worse outcome.36

CTAs performed <96 hours from symptom onset have a high accuracy for predicting underlying vascular anomalies, with sensitivities ≥95% and specificities approaching 100%. Positive and negative predictive values have also been reported to be in excess of 97%.37,38 Even so, CTA exposes patients to the risks of radiation, as well as risks associated with contrast-induced nephropathy (CIN) and allergic reaction, which can lead to death. Furthermore, the risk of contrast on blood–brain barrier permeability has unknown effects on bleeding risks and the worsening of vasogenic edema.39–43

CIN is defined as a 25% elevation from baseline serum creatinine levels or an absolute increase of 0.5 mg/dL <48 to 72 hours of contrast administration.44 CIN is associated with

<table>
<thead>
<tr>
<th>Phase of Blood</th>
<th>NCCT</th>
<th>T1-Weighted MR</th>
<th>T2-Weighted MR</th>
<th>T2*-Weighted MR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperacute</td>
<td>Oxyhemoglobin</td>
<td>Smooth, hyperdense</td>
<td>Hypointense or isointense</td>
<td>Hyperintense</td>
</tr>
<tr>
<td>Acute (12–48 h)</td>
<td>Deoxyhemoglobin</td>
<td>Hyperdense with fluid levels</td>
<td>Isointensity or slight hypointensity with thin hyperintense rim in the periphery</td>
<td>Hyperintense with hyperintense perilesional rim</td>
</tr>
<tr>
<td>Early subacute (72 h)</td>
<td>Methemoglobin intracellular</td>
<td>Hypodense region of edema with mass effect</td>
<td>Hyperintensity</td>
<td>Hyperintensity</td>
</tr>
<tr>
<td>Late subacute (3–20 d)</td>
<td>Methemoglobin extracellular</td>
<td>Less intense with ring-like profile</td>
<td>Hyperintensity</td>
<td>Hyperintensity</td>
</tr>
<tr>
<td>Chronic (9 wk)</td>
<td>Hemosiderin and ferritin</td>
<td>Isodense or modest confined hypodensity</td>
<td>Hypointensity</td>
<td>Hyperintensity</td>
</tr>
</tbody>
</table>
5-fold higher risks of prolonged hospitalization and mortality.\textsuperscript{45-47} In an emergency setting, it is neither feasible to adopt preventive measures such as prehydration with the addition of acetylcysteine\textsuperscript{48} nor possible to fully know patient history. However, the incidence of CIN, even in emergency settings, has been reported to be low (2\%).\textsuperscript{49}

### Magnetic Resonance

Stroke MR protocols should include T1, T2, T2* or gradient echo (GE), fluid-attenuated inversion recovery, contrast-enhanced, diffusion-weighted, and perfusion-weighted images, as well as MR angiography.\textsuperscript{50} The appearance of ICH on MR is primarily affected by the age of hematoma, as well as the type of MR contrast used. The substrate responsible for early hemorrhage identification on MR scan is deoxyhemoglobin, a blood degradation product with paramagnetic properties, because of its unpaired electrons. On GE images, a few areas of hyperintensity can be detected in the lesion core, and of these, most are usually surrounded by hypointense boundaries. Hyperintense signals are commonly found bordering the central lesion on T2-weighted and GE images, whereas a hypointense signal is commonly observed on T1-weighted images, thereby indicating perifocal vasogenic edema.\textsuperscript{50}

There is strong evidence supporting the diagnostic accuracy of MR in the hyperacute setting\textsuperscript{51,52} even after only 20 minutes of symptom onset.\textsuperscript{53} A randomized trial investigating the role of MR in detecting ICH\textsuperscript{64} has reported that hyperacute ICH is detectable with excellent accuracy even when the raters had only limited experience. Moreover, GE is as sensitive as NCCT in the detection of acute ICH, whereas a complete MR in patients with acute stroke has higher sensitivities for IS (diffusion-weighted imaging sequences) and chronic hemorrhage.\textsuperscript{55,56} However, in the case of minor bleeding, GE MR may not be sufficient to distinguish acute bleeding from chronic bleeding (ie, microbleeds [MBs]), and for this, NCCT should be performed.\textsuperscript{58} Furthermore, patient factors (ie, clinical instability, presence of pacemaker, claustrophobia) and hospital factors (availability of MR) may cause obtaining an MR impossible or impractical in the acute setting, and therefore, NCCT remains the neuroimaging modality of choice for the diagnosis of acute stroke.\textsuperscript{57,58}

MR is also a neuroradiological tool for distinguishing between hemorrhagic transformation and primary ICH. In fact, most HTs are smaller than their fields of ischemic infarct; thus, MR can provide information on nonhemorrhagic regions and evidence whether blood is within the larger ischemic infarct.\textsuperscript{59} A primary hematoma tends to be round and have a larger surrounding edema than would be seen on IS. Furthermore, hematomas do not necessarily respect vascular territories.\textsuperscript{59} In case of hemorrhagic transformation of IS, MR angiography can identify the location of vascular occlusion.

MR has a high diagnostic rate for detecting underlying causes of secondary hemorrhages, including vascular malformations, tumors, and cerebral vein thrombosis, as well as a high diagnostic yield for young patients having lobar ICH and no history of hypertension.\textsuperscript{60} Thus, MR is the most sensitive tool for detecting cerebral venous thrombosis in the acute, subacute, and chronic phases.\textsuperscript{66} Contrast-enhanced MR venography is able to show the thrombosed segment of the venous sinus and is generally well correlated with conventional angiographic findings.\textsuperscript{66} It also assists in distinguishing anatomic variants, such as a hypoplastic sinus, from cerebral venous thrombosis.\textsuperscript{67}

MR is the most sensitive and specific neuroradiologic modality for detecting cavernomas, the abnormal capillary-like vessels with intermingled connective tissue whose rupture can lead to ICH.\textsuperscript{64} Cavernoma has a hyperintense popcorn ball–like appearance at T2-weighted imaging. The central component, hyperintense, indicates subrecent bleeding; the hypointense halo consists of hemosiderin and is the outcome of remote bleeding.

With MR, it is possible to detect previously existing and clinically silent cerebral MBs that are not detectable on CT. MBs provide a lifetime history of hemorrhage. MBs are small dot-like lesions having a hypointense appearance on GE sequences and are usually smaller than 5 to 10 mm (Figure 2). Pathological studies have proven that MBs correspond to hemosiderin-laden macrophages adjacent to small vessels, suggesting previous extravasations of blood. MBs can have numerous types of mimics, such as the calcification of the basal ganglia, diffused axonal injury, metastatic melanoma, cavernous malformation, and small perforating arteries.\textsuperscript{65} MBs are considered markers of vascular pathology, including hypertensive vasculopathy and CAA, as identified from histopathologic analyses of the vessels surrounding MBs. Furthermore, MBs have been reported to be predictors of ICH in prospective observational studies on both ICH\textsuperscript{66,67} and IS.\textsuperscript{68,69} MBs can indicate bleeding-prone angiopathy and a high rate of hemorrhagic transformation in patients on anticoagulation, antithrombotic, or thrombolytic therapies.\textsuperscript{70} However,
MBs are thought to be more than markers for minor episodes of cerebrovascular extravasation. In fact, a recent pathological study by Janaway et al. has reported that a large putamen haemosiderin, correlated with more MBs, was significantly associated with putaminal indices of small-vessel ischemia (microinfarcts, arteriolosclerosis, perivascular attenuation), as well as lacunes in each examined brain region but neither with large-vessel disease nor whole-brain neurodegenerative pathologies. These findings suggest that basal ganglia MR MBs are a surrogate for ischemic small-vessel disease rather than exclusively a hemorrhagic diathesis.

Lobar localization of MBs and their associations with lobar ICH, especially in the elderly patients, render MBs possible indicators of CAA. To this regard, the Boston criteria for probable CAA specify that this diagnosis should not be made when MBs are located in the basal ganglia, thalamus, or brain stem, the regions atypical for CAA pathology.

**Catheter Angiogram**

Subarachnoid hemorrhage, atypical (noncircular) hematoma configuration, edema out of proportion seen on CT at admission, unusual hemorrhage location, or the presence of other abnormal structures in the brain, including masses, are all distinctive radiological features of secondary causes of ICH. In these cases, a catheter angiogram is necessary to best reveal underlying conditions, including arteriovenous malformations, Moyamoya disease, tumors, vasculitis, reversible cerebral vasoconstriction syndrome, and cerebral vein thromboses.

Angiography may also be indicated in patients with no obvious cause of bleeding. The angiographic yield has shown to be significantly high in young patients without pre-existing hypertension. Young age followed by the absence of hypertension and lobar hemorrhage have been proven to be the main factors influencing diagnostic choices in clinical practice. The presence of intraventricular hemorrhage in patients with acute spontaneous ICH is not associated with an increased risk of an underlying vascular lesion and should not be used to select patients for neurovascular evaluation. Timing of cerebral angiography should take into consideration the clinical state of the patient and the neurosurgeon’s judgment regarding urgency of surgery. There is a tendency to perform diagnostic investigations <1 or 2 days in younger patients. Delayed angiography can also show unexpected underlying structural lesions in patients without radiological suspicion of secondary causes of ICH, and therefore, a follow-up angiography should be considered for all patients with a first-negative angiogram, in the absence of a specific cause of hemorrhage.

MR angiogram/venogram along with CT angiogram/venogram are reliable tools for confirming secondary causes of hemorrhage. Thus, these are reliable substitutes for catheter angiogram, which is an invasive procedure that is not always readily available. In fact, catheter angiogram is associated with the risks of transient and permanent neurological deficits, 0.9% and 0.5%, respectively. It is expensive and time- and labor-intensive, as well as requires patient cooperation, a stable patient condition, and continuous monitoring. Radiation doses of catheter angiography (5 times higher than CTA) are delivered to both patients and operators. For this reason, CTA should be considered the better initial screening approach for identifying secondary vascular lesions, compared with catheter angiogram. Nonetheless, catheter angiogram remains the diagnostic tool of choice for the treatment of aneurysms and arteriovenous malformation (Figure 3).

![Figure 3. Catheter angiogram: Left temporal arteriovenous malformation before and after treatment (black arrows).](http://stroke.ahajournals.org/)

![Figure 4. Diagnostic work-up flowchart of intracerebral hemorrhage.](http://stroke.ahajournals.org/)
Conclusions
An optimal neuroradiological diagnosis and management of ICH requires more than defining the size, location, and presence of intraventricular blood. In fact, knowing the causes of ICH will allow us to better diagnose and treat ICH. Specifically, the pathogenesis provides more accurate information on predictive factors that can influence the clinical outcome and mortality: risk of hematoma expansion, presence of underlying diseases, and previous lesions such as MBs.

Here, we propose a diagnostic flowchart that incorporates size, location, clinical risk factors, and pathogenesis that, when considered together, can lead to a more accurate diagnosis and, thus, a better management of ICH (Figure 4). Regarding those who may do without further imaging work-up, this decision, according to the authors, should be based on a careful assessment of age, functional outcome, life expectancy, as well as the will of the patient.

Disclosures
Dr Caso received honoraria as a member of the speaker bureau and advisory board of Boehringer Ingelheim. The other authors have no conflicts to report.

References
36. Aviv RI, Gladstone D, Goldstein J, Flaherty M, Broderick J, Demchuk A; Spot Sign for Predicting and Treating ICH Growth and Spot Sign


**Keywords**: CT angiography | CT scan | digital angiography | intra-cerebral hemorrhage | MR
Neuroimaging in Intracerebral Hemorrhage
Federica Macellari, Maurizio Paciaroni, Giancarlo Agnelli and Valeria Caso

Stroke. 2014;45:903-908; originally published online January 14, 2014;
doi: 10.1161/STROKEAHA.113.003701
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2014 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/45/3/903

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org//subscriptions/