Preventing air microembolism in cerebral angiography: a *JNIS* fellow's perspective

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TINY BUBBLES IN THE LINE

Digital subtraction angiography is arguably the most valuable tool in the diagnosis and treatment of cerebrovascular disease. How benign is this procedure? Every fellow is taught their mentor's semi-unique process of checking lines, clearing syringes, and preventing air embolism. Neurointerventional research is generally focused on safer technology, clinical outcomes, and quality improvement. Understanding air microemboli remains important for optimized neurointerventional practice. Studies from over 20 years ago first confirmed a high incidence of microemboli in cerebral angiography, but little has evolved in the techniques used to prepare and flush lines and syringes since. A prospective study in 1999 found new clinically-silent MRI diffusion weighted imaging (DWI) lesions in 23% of patients undergoing cerebral angiography.[1] Another study showed that 28% of subjects undergoing diagnostic cerebral angiography had new DWI lesions, and 20% of these persisted as fluid attenuated inversion recovery (FLAIR) lesions at follow-up.[2] In interventional cardiology, transcranial Doppler (TCD) monitoring in patients undergoing percutaneous transluminal coronary angioplasty showed cerebral microemboli signals in all patients. More than 70% of TCD microemboli signals occurred during injections and were not correlated to the extent of aortic atheroma or to clinical events, pointing to a gaseous origin.[3]

INNOCUOUS OR INSIDIOUS?

Many studies label angiography-related DWI lesions or detection of Doppler signals as subclinical or 'silent'" because no acute neurologic change is detected post-procedurally. However, new post-procedural DWI lesions in patients undergoing carotid interventions were associated with significant memory decline.[4] In the cardiac surgery literature, air microemboli after cardiac bypass surgery utilizing a heart lung machine had significant clinical effects. These new, post-procedural DWI lesions were associated with neurocognitive decline and a significant relative reduction in prefrontal activation on functional MRI.[5 6] Though not focal or immediately apparent, the accumulation of these neurocognitive insults in patients undergoing repeated angiography may be causing unrealized harm. It is time to re-examine this problem and modernize the approach to reducing avoidable air microembolism.

THE PHYSICS OF BUBBLES

The physics of bubble formation in solution offers insight into the causes and potential solutions of air microembolism. Gases in solution exist either in dissolved or undissolved states. In specific conditions, gas molecules leave solution, coalesce, and form bubbles. There are several factors that play a part in bubble formation in angiography. The solubility of gas decreases as a solution's salt concentration increases, therefore saline solution will have more undissolved gas than hypotonic solution. Gas solubility is also decreased by increasing temperatures. In the case of refrigerated heparinized saline bags, bubbles form in the lines as the saline warms to room temperature. Bernoulli's principle explains how, as heparinized saline solution flows from the pressurized bags and ultimately into the catheter, the changes in tube diameter and velocity affect the pressure of the solution. If the pressure of the fluid drops below its vapor pressure, bubbles form through cavitation and coalescence. The salt ions in saline act as additional bubble nucleation sites and reduce surface tension by disrupting the hydrogen bonds between water molecules, making it easier for air bubbles to form.[7]

THE DEVIL IS IN THE DETAILS

In their earliest days of training, neurointerventional fellows are taught to practice meticulous bubble hygiene by examining lines and syringes. Despite this vigilance, air microembolism still occurs, as evidenced by DWI lesions on post-angiography MRI. Though neuroendovascular technology is advancing at an incredible rate, many of the techniques, devices, and principles for avoiding air microemboli that are currently being used were described decades ago and have not been thoroughly investigated since. Thirty years ago, it was established that there was no difference in using glass versus plastic syringes in reducing bubbles and air emboli, therefore, plastic syringes are now used universally.[8]

Interestingly, some of the more historic papers do not support current methods. The commonly used and convenient closed-flush manifold system for filling syringes, for example, may be responsible for some microemboli. Theoretically, the negative pressure generated with the closed-flush manifold creates cavitation microbubbles within the syringe that then coalesce on the walls and are dislodged during hand injection. An in vitro study using an in-line bubble trap and standard angiographic techniques supports this concept, finding that more bubbles are captured in the inline trap when syringes were filled with a closed-flush manifold compared with an open basin.[9] A study by Markus *et al* used TCD monitoring during angiography and found that air was primarily introduced while drawing contrast into the syringe and during injections. Markus also found that the amount of air detected was significantly reduced by slow injection of saline and contrast into the catheter.[10] This is readily explained by Bernoulli's principle, as the velocity and pressure of non-compressible, non-viscous fluids are inversely proportional to each other, so a faster injection may draw gas out of solution within the catheter itself. Monitoring and reducing the flow rate of the flush lines can prevent sudden changes in pressure that may lead to cavitation bubbles and surface agitation in the drip chamber.

The role of power injectors, particularly in three-dimensional rotational angiography (3DRA), is also another source for cavitation bubble formation during preparation or injection of contrast. A recent survey of

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neuroradiologists in the USA and Canada showed great variability in their power injection rates and volumes. The majority (81.4%) of the surveyed neurointerventionalists also believed that power injection rates do not significantly contribute to complications during angiography.[11] Most studies on air embolism in cerebral angiography uses hand injection of contrast, and understanding the unique contribution power injectors may play in air embolism is important as 3DRA is increasingly utilized in diagnostic angiography.

CATCHING BUBBLES

Though injection technique and operator diligence may help reduce microemboli, the development of new tools to avoid these and other complications will ultimately make cerebral angiography safer. As discussed previously, the cardiac literature has correlated clinically significant neurocognitive decline with cerebral gaseous microemboli in patients undergoing cardiac bypass using the heart lung machine.[4 5 12] The addition of arterial line filters in cardiopulmonary bypass circuits reduced gaseous microemboli and neuropsychologic impairment and has since become a standard in cardiac bypass surgery worldwide.[12–15] Perthel *et al* found that insertion of an inline arterial dynamic bubble trap in cardiac bypass circuit tubing reduced microbubbles by 65% and TCD microembolic signals in the middle cerebral artery by 86%.[14] A prospective study compared post-procedural DWI lesions in patients undergoing cerebral angiography with and without the addition of air microemboli filters placed between the catheter and flush line and the catheter and contrast injection port. The study found that use of the filters reduced DWI lesions detected on MRI from 22% in the control group to 6% in the air filter group.[16] There are commercially available inline filters that could be utilized to investigate the role of air filters in cerebral angiography, but ultimately a device made specifically for this application would be the most effective solution.

CONCLUSION

Safe angiography is the cornerstone of neurointerventional practice and the literature has shown that cerebral microemboli are neither subclinical nor benign. Understanding the physics of bubble formation provides some insights, but despite meticulous efforts, iatrogenic air microembolism remains a risk for cumulative neurocognitive deficits. Arterial line filters reduce cerebral microemboli in cardiac surgery, and neuroendovascular-specific air filtration devices hold promise but require further research and development. By harnessing technology and engaging industry, previous generations of fellows have become the Promethean pioneers of our field, advancing endovascular indications and devices. As the current generation of fellows venture into practice, we inherit the responsibility to collaborate and develop innovative solutions to the fundamental challenges impeding improved patient safety in neurointervention.

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