Reply:

G. Cattaneo, M. Schumacher, G. Trummer, H. Urbach and S. Meckel

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REPLY:

We would like to comment on the letter by our colleagues Mattingly et al regarding our article "Endovascular Cooling Catheter for Selective Brain Hypothermia: An Animal Feasibility Study of Cooling Performance."[1] We appreciate the innovative research by Mattingly et al,[2] who have studied a novel catheter system dedicated to selective brain hypothermia in their recently published work. In our above-referenced article, we have underlined the cooling performance of the extracorporeal blood cooling system described in Mattingly et al[2] with regard to the depth and velocity of the provided brain hypothermia.

Our endovascular approach for selective brain cooling is different in many respects from the technique presented by Mattingly et al. We aimed for a combination of selective brain cooling with mechanical thrombectomy for treatment of acute stroke related to large cerebral artery occlusion. Therefore, the inner coolant circuit of our catheter system provides for blood cooling independent of the larger central working lumen. The latter is dedicated to mechanical thrombectomy only and permanently allows stent-retriever placement and clot retrieval under aspiration without interfering with the cooling performance. Thus, our system can provide a very early selective brain hypothermia initiated before recanalization and extended during and after the critical phase of reperfusion; this system represents, in our view, a paradigm shift compared with recently favored postreperfusion cooling approaches. This "cold reperfusion" approach may allow early neuroprotection by addressing specific inflammatory pathways of ischemia and reperfusion insult as depicted by Pan et al,[3] presumably increasing the therapeutic window for recanalization techniques in the future.

The TwinFlo catheter (ThermopeutiX, San Diego, California) system as described by Mattingly et al consists of a 14F outer catheter placed into the descending aorta and a 9.5F inner catheter with a balloon at the tip, placed into the common carotid artery, which supplies the ischemic hemisphere. In our understanding of the presented work, the inner lumen of 2-mm diameter is not free for use in mechanical thrombectomy and aspiration during cooling because it is needed for the inflow of cooled blood from the extracorporeal cooling circuit. We agree that the size of the inner catheter lumen is suitable for standard access to the intracranial vessels in a mechanical thrombectomy procedure. However, interruption of this extracorporeal blood circuit during the procedure may impose a high risk of catheter thromboembolism or generation of thrombus within the blood pump components, even with short periods of blood stasis. Thus, extracorporeal blood cooling may only be initiated after successful recanalization of the occluded cerebral artery in the postreperfusion phase as it was presented in the study of a swine model with focal ischemia due to transient MCA branch occlusion.[2]

With regard to the optimal target temperature for brain hypothermia in acute stroke treatment, Mattingly et al referred to an older study published in 1955 that described the reduction of metabolic demand in the hypoperfused brain, which decreased almost "linearly" with the reduction in temperature.[4] However, this finding represents only one of the multiple proposed neuroprotective effects of therapeutic hypothermia in cerebral ischemia, including a reduction of detrimental neuroinflammatory responses, suppression of neurotransmitter release, attenuation of neuronal apoptosis, and dampening of free radical generation.[5] Recent in vivo studies with ischemic models, clinical studies, and guidelines for patients with cardiac arrest put more emphasis on mild therapeutic hypothermia with target temperatures between 33°C and 35°C, which aim at a balance between the neuroprotective effects and the control of adverse events, for implementation in clinical practice.[6,7] In our experimental study, we demonstrated that systemic temperatures followed local brain temperatures in selective intracarotid blood cooling with a relatively stable temperature gradient. The lower brain temperatures of <30° achieved within 15 minutes by extracorporeal blood cooling, which were described in the work of Mattingly et al, involve important issues in the management of patients with stroke, such as infection, shivering, and coagulation impairment[8] due to high-dose heparinization. These issues have to be weighed against the potential benefits of an assumed stronger neuroprotection related to a lower metabolic demand.

We esteem the work of Mattingly et al, who have shown an exciting approach for selective brain hypothermia in acute stroke treatment. Applying 3 hours of early postreperfusion cooling, they could demonstrate, in a swine model, a marked reduction of infarct volume by 42% of transient MCA branch occlusion. Our approach aims at simultaneous neuroprotection in patients with acute large-artery occlusions (MCA M1 or terminal ICA) that undergo endovascular mechanical thrombectomy as a standard treatment. Thus, it should not interfere or delay the standard endovascular procedure and at the same time provide selective brain hypothermia with limited systemic effects and minimized influence on management of patients with stroke. Currently, both approaches may coexist until further validation in a clinical context in patients with acute stroke has been performed.

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G. Cattaneo
Acandis GmbH and Co. KG
Pforzheim, Germany
M. Schumacher
Department of Neuroradiology
G. Trummer
University Heart Center
H. Urbach
S. Meckel
Department of Neuroradiology
University Hospital Freiburg,
Freiburg, Germany