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LETTER TO THE EDITOR

N-Butyl Cyanoacrylate–Lipiodol Mixture for Endovascular Purpose: Polymerization Kinetics Differences Between In Vitro and In Vivo Experiments

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To the Editor,

We recently read with great interest the article by Hayashi et al. [1] recently published in *CVIR* and evaluating the polymerization time and flow cessation time of a *N*-butyl cyanoacrylate (NBCA)–Lipiodol mixture in an in vitro model. We have several comments. First of all, we would like to congratulate the authors for their experimental study using both a static model and a pulsating flow model. Little is known regarding the polymerization time of NBCA/Lipiodol after injection, and a risk exists of excessive or incomplete embolization or adhesion of the catheter tip to the vascular wall. The ratio is empirically decided by the interventional radiologist considering several parameters. However, the optimal ratio may not be constant and may differ depending on the blood vessel diameter, blood velocity, and distance from the microcatheter tip to the target [2]. In this study, polymerization time prolonged as the NBCA concentration decreased and the flow cessation time was shorter than the polymerization time for all ratio samples.

Discrepancy between properties in vitro and embolization effect in vivo of various ratios of NBCA/Lipiodol may be explained by several factors. First, the authors described injection of saline flushed through the catheter in the flow model, followed by injection of NBCA/Lipiodol. We are very surprised by the use of saline to flush the microcatheter before glue injection, considered as a fluid rich in ions that can start polymerization. Indeed, before injecting glue, the microcatheter is usually flushed with 5% dextrose to prevent premature polymerization of the mixture triggered by anions from residual blood or saline. Second, it is well known that with the increased amount of Lipiodol, the polymerization time increased. It may explain why in vivo experiments showed embolization occurring more distally at a 1:3 ratio than at a 1:1 ratio. At the same time, both the viscosity of NBCA/Lipiodol and the area of the polymer increase, explaining why no difference could be found between 1:3 and 1:9 ratios in vivo, where polymerization time and viscosity greatly changed in vitro [3]. Indeed, increased viscosity obtained with a high ratio of Lipiodol may disproportionately reduce blood flow within small arteries, resulting in a relatively limited degree of peripheral embolization. Third, the kinetics of NBCA/Lipiodol mixture may be modified by not only polymerization time and viscosity but also other factors, including blood vessel diameter, blood velocity, and blood pressure and their combination, which remain to be evaluated. Additionally, two steps have been described in the polymerization process: a fast polymerization at the interface between the glue and the liquid with which it is in contact, and then a slower polymerization of the cast volume where a reaction front spreads into the mixture [4].

Last, the blood products, especially the red blood cells but also triglycerides, increase the polymerization rate, even more than the plasma. On one hand, the PVA tube of flow model may increase the polymerization time of NBCA/Lipiodol compared with human vascular endothelium, resulting in shorter polymerization time than in vivo

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results; on the other hand, the use of Lipiodol in vitro may inhibit the contact between NBCA and blood, meaning that the polymerization time and the flow cessation during embolization of blood vessels in vivo might be shorter than the results in vitro because of more likely contact between NBCA/Lipiodol and blood.

In conclusion, several factors may influence the NBCA/Lipiodol polymerization explaining the kinetics differences between in vitro and in vivo experiments.

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical Approval This article does not contain any studies with human participants or animals performed by any of the authors.

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