



**HAL**  
open science

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

Romarc Loffroy, Pierre-Olivier Comby, Kévin Guillen, Anne-Virginie Salsac

► **To cite this version:**

Romarc Loffroy, Pierre-Olivier Comby, Kévin Guillen, Anne-Virginie Salsac. N-Butyl Cyanoacrylate–Lipiodol Mixture for Endovascular Purpose: Polymerization Kinetics Differences Between In Vitro and In Vivo Experiments. *CardioVascular and Interventional Radiology*, 2020, 43 (9), pp.1409-1410. 10.1007/s00270-020-02540-3 . hal-02816630

**HAL Id: hal-02816630**

**<https://utc.hal.science/hal-02816630v1>**

Submitted on 6 Jun 2020

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

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

**Romaric Loffroy, Pierre-Olivier Comby,  
Kévin Guillen & Anne-Virginie Salsac**

**CardioVascular and Interventional  
Radiology**

ISSN 0174-1551

Cardiovasc Intervent Radiol  
DOI 10.1007/s00270-020-02540-3



**Your article is protected by copyright and all rights are held exclusively by Springer Science+Business Media, LLC, part of Springer Nature and the Cardiovascular and Interventional Radiological Society of Europe (CIRSE). This e-offprint is for personal use only and shall not be self-archived in electronic repositories. If you wish to self-archive your article, please use the accepted manuscript version for posting on your own website. You may further deposit the accepted manuscript version in any repository, provided it is only made publicly available 12 months after official publication or later and provided acknowledgement is given to the original source of publication and a link is inserted to the published article on Springer's website. The link must be accompanied by the following text: "The final publication is available at [link.springer.com](http://link.springer.com)".**



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

Romaric Loffroy<sup>1</sup> · Pierre-Olivier Comby<sup>1</sup> · Kévin Guillen<sup>1</sup> · Anne-Virginie Salsac<sup>2</sup>

Received: 8 May 2020 / Accepted: 25 May 2020

© Springer Science+Business Media, LLC, part of Springer Nature and the Cardiovascular and Interventional Radiological Society of Europe (CIRSE) 2020

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

✉ Romaric Loffroy  
romaric.loffroy@chu-dijon.fr

<sup>1</sup> ImViA Laboratory-EA 7535, Department of Vascular and Interventional Radiology, Image-Guided Therapy Center, François-Mitterrand University Hospital, 14 Rue Gaffarel, BP 77908, 21079 Dijon Cedex, France

<sup>2</sup> Biomechanics and Bioengineering Laboratory, UMR CNRS 7338, Compiègne Technology University, Sorbonne University, Compiègne, France

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.

**Funding** This study was not supported by any funding.

**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.

## References

1. Hayashi N, Takeuchi Y, Miura H, et al. Is the cessation of blood flow faster than the polymerization of an *N*-butyl cyanoacrylate–lipiodol mixture? An in vitro phantom study. *Cardiovasc Interv Radiol.* 2020;43:630–5.
2. Loffroy R, Guiu B, Cercueil JP, Krausé D. Endovascular therapeutic embolisation: an overview of occluding agents and their effects on embolised tissues. *Curr Vasc Pharmacol.* 2009;7:250–63.
3. Takasawa C, Seiji K, Matsunaga K, et al. Properties of *N*-butyl cyanoacrylate-iodized oil mixtures for arterial embolization: in vitro and in vivo experiments. *J Vasc Interv Radiol.* 2012;23:1215–21.
4. Li YJ, Barthès-Biesel D, Salsac AV. Polymerization kinetics of *N*-butyl cyanoacrylate glues used for vascular embolization. *J Mech Behav Biomed Mater.* 2017;69:307–17.

**Publisher's Note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.