



## University of Groningen

### Reply

van Dongen, Joris A; Willemsen, Joep C N; Spiekman, Maroesjka; Vermeulen, Karin M; Harmsen, Martin C; Stevens, Hieronymus P; van der Lei, Berend

*Published in:*  
Plastic and Reconstructive Surgery

*DOI:*  
[10.1097/PRS.0000000000004930](https://doi.org/10.1097/PRS.0000000000004930)

**IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.**

*Document Version*  
Final author's version (accepted by publisher, after peer review)

*Publication date:*  
2018

[Link to publication in University of Groningen/UMCG research database](#)

*Citation for published version (APA):*

van Dongen, J. A., Willemsen, J. C. N., Spiekman, M., Vermeulen, K. M., Harmsen, M. C., Stevens, H. P., & van der Lei, B. (2018). Reply: The Addition of Platelet-Rich Plasma to Facial Lipofilling: A Double-Blind, Placebo-Controlled, Randomized Trial. *Plastic and Reconstructive Surgery*, 142(5), 796E-798E. <https://doi.org/10.1097/PRS.0000000000004930>

#### Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

#### Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

**Reply to: “The addition of Platelet-rich Plasma to facial lipofilling: A Double-Blind, Placebo-Controlled, Randomized Trial.”**

Joris A. van Dongen, B.Sc<sup>1,2,3</sup>, Joep C.N. Willemsen, MD<sup>1,2,3</sup>, Maroesjka Spiekman, MD<sup>1</sup>, Karin M. Vermeulen, PhD<sup>4</sup>, Martin C. Harmsen, PhD<sup>1</sup>, Hieronymus P. Stevens, MD, PhD<sup>3</sup>, Berend van der Lei, MD, PhD<sup>2,5,\*</sup>

<sup>1</sup> Department of Pathology & Medical Biology, University of Groningen and University Medical Center Groningen, Groningen, the Netherlands

<sup>2</sup> Department of Plastic Surgery, University of Groningen and University Medical Center Groningen, Groningen, the Netherlands

<sup>3</sup> Bergman clinics, Location Rijswijk, the Netherlands

<sup>4</sup> Department of Epidemiology, University Medical Center Groningen, University of Groningen, Groningen, the Netherlands

<sup>5</sup> Bergman Clinics, locations Heerenveen, Zwolle and Groningen, the Netherlands

**\*Corresponding author:** Dr. Hieronymus P. Stevens, MD, PhD, Bergman Clinics, Rijswijk Braillelaan 5, 2289 CL, Rijswijk, the Netherlands. Tel: 131624810440, Fax: 010-4471884, Email: [stevens.hp@gmail.com](mailto:stevens.hp@gmail.com)

**Conflict of interest:** None of the authors has a financial interest in any of the products, devices or drugs mentioned in this manuscript.

Sir,

We thank the authors for their interesting and valuable comments on our recent published article: “The addition of Platelet-rich Plasma to facial lipofilling: A Double-Blind, Placebo-Controlled, Randomized Trial.”<sup>1</sup> We fully agree with their comment that future prospectively randomised clinical studies are warranted to evaluate the concentration-dependent effect of Platelet-rich Plasma (PRP) on adipose derived stromal cells (ASC) in combination with facial lipofilling.<sup>2</sup> However, some of their other well appreciated comments need to be addressed.

In our prospective study presented, we concluded that the addition of PRP to facial lipofilling significantly reduced postoperative recovery time but did not improve clinical parameters like skin elasticity and patient satisfaction.<sup>1</sup> Though, a regression analysis of the true skin elasticity as a function of age showed a negative correlation preoperative. After applying facial lipofilling with and without PRP the correlation reversed, with a stronger positive correlation in the PRP group. This difference was, however, not significant, possible due to the small sample size. In this study, PRP was mixed with adipose tissue in a 12:1 ratio. In an earlier retrospective study (2014) published by our group, we found that the addition of PRP to facial lipofilling in combination with or without a MACS-lift also significantly reduced recovery time. In contrast to our prospective study presented, also an improved aesthetic outcome was observed. In this retrospective study, PRP was mixed with adipose tissue in a 10:1 ratio.<sup>3</sup>

The authors state that the lack of significance of the effect observed in our prospective trial might be due to decreased PRP concentrations relative to the amount of adipose tissue.<sup>2</sup> The slightly different ratio in our prospective study cannot, to our opinion, explain the difference in aesthetic outcome; this latter has to be ascribed to the retrospective nature of this study without the use of more objective and validated instruments like the cutometer.<sup>4</sup> Definite proof of clinical aspects can only be clearly found in prospective studies.

In our latest *in vitro* study we found that a high concentration of PRP (*i.e.* 15%) resulted in an eight-fold increased proliferation of ASC.<sup>5</sup> However, as the authors mentioned, a lower concentration of PRP (*i.e.* 5% PRP) was shown to be more beneficial for wound healing purposes as compared to the higher concentration of PRP.<sup>5</sup> A lower concentration of PRP resulted in an increased expression of genes that encode paracrine factors by ASC such as collagen 1, matrix metalloproteinase (MMP) 1 and 2 as well as a decreased gene expression of tissue inhibitor metalloproteinase 1 (TIMP1). Collagen 1 is important in dermal scar formation, while MMP1 as well as MMP2 are essential natural collagenases which are key players in tissue remodelling. Moreover, MMP1 and MMP2 are inhibited by TIMP1 and therefore a reduced expression of TIMP1 may augment tissue remodelling.<sup>5</sup> Based on the aforementioned reasons, it might even be possible that the concentration of PRP used in the prospective trial was too high and a lower concentration of PRP should have been used. Nevertheless, we caution that the clinical translation of the results of our previous *in vitro* study with PRP is at best an educated guess. The ASC in our study were cultured, which means that their phenotype differs from their tissue-resident precursors. We cannot presume that PRP influences the proliferation of tissue-resident ASC, while their secreted products may be influenced as is the production of secreted factors by other tissue-resident cells such as fibroblasts, smooth muscle cells, endothelial cells and adipocytes too. The net effect of exogenously administered PRP is the sum of the influences on everyone of the cell types. It is a flaw of reasoning to reduce the efficacy of lipoaspirates to their ASC precursors.

There is quite obvious a definite need for more prospective randomized clinical trials to evaluate the effect of different concentrations of PRP on facial lipofilling. Up till then, we can only conclude that PRP mixed to facial lipofilling (12:1) will only shorten recovery time, without improving the superficial skin elasticity and patient satisfaction.

## References

1. Willemsen JCN, Van Dongen J, Spiekman M, et al. The Addition of Platelet-Rich Plasma to Facial Lipofilling: A Double-Blind, Placebo-Controlled, Randomized Trial. *Plastic and reconstructive surgery*. 2018;141(2):331-343.
2. Ozer K, Atan O. The Addition of Platelet-Rich Plasma to Facial Lipofilling: A Double-Blind, Placebo-Controlled, Randomized Trial. *Plastic and reconstructive surgery*. 2018.
3. Willemsen JC, van der Lei B, Vermeulen KM, Stevens HP. The effects of platelet-rich plasma on recovery time and aesthetic outcome in facial rejuvenation: preliminary retrospective observations. *Aesthetic plastic surgery*. 2014;38(5):1057-1063.
4. Nedelec B, Forget NJ, Hurtubise T, et al. Skin characteristics: normative data for elasticity, erythema, melanin, and thickness at 16 different anatomical locations. *Skin research and technology : official journal of International Society for Bioengineering and the Skin (ISBS) [and] International Society for Digital Imaging of Skin (ISDIS) [and] International Society for Skin Imaging (ISSI)*. 2016;22(3):263-275.
5. Willemsen JC, Spiekman M, Stevens HP, van der Lei B, Harmsen MC. Platelet-Rich Plasma Influences Expansion and Paracrine Function of Adipose-Derived Stromal Cells in a Dose-Dependent Fashion. *Plastic and reconstructive surgery*. 2016;137(3):554e-565e.