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Prediction formulas to determine breast cancer treatment related lymphedema do have a clinical relevance

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1 Prediction formulas to determine breast cancer treatment related lymphedema do have a clinical
2 relevance.

3 (response to letter by Fangdi Sun et al. to “Current and future perspectives on the evaluation,
4 prevention and conservative management of breast cancer related lymphoedema: a best practice
5 guideline”)

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7 A response written and approved by all authors of the original manuscript:

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9 Nick Gebruers^{1,2,7}, Hanne Verbelen¹, Tessa De Vrieze^{1,4}, Lore Vos⁴, Nele Devoogdt^{4,5}, Lore Fias^{2,6},
10 Wiebren Tjalma^{2,3,7}

- 11 1. University of Antwerp, Faculty of Medicine and Health Sciences, department of rehabilitation
12 sciences and physiotherapy, MOVANT research group, Universiteitsplein 1, 2610 Wilrijk,
13 Belgium (nick.gebruers@uantwerpen.be; hanne.verbelen@uantwerpen.be;
14 tessa.devrieze@student.uantwerpen.be)
- 15 2. Multidisciplinary oedema clinic, University of Antwerp and Antwerp University hospital;
16 Wilrijkstraat 10, 2650 Edegem (Nick.gebruers@uantwerpen.be, Wiebren.tjalma@uza.be,
17 Lore.fias@uza.be)
- 18 3. University of Antwerp, Faculty of Medicine and Health Sciences, department of medicine,
19 Universiteitsplein 1, 2610 Wilrijk, Belgium (wiebren.tjalma@uza.be)
- 20 4. KU Leuven - University of Leuven, Department of Rehabilitation Sciences, Herestraat 49,
21 3000 LEuven (lore.vos@kuleuven.be, tessa.devrieze@kuleuven.be,
22 nele.devoogdt@KUleuven.be)
- 23 5. University Hospitals Leuven, Department of Vascular Surgery and Department of Physical
24 Medicine and Rehabilitation, Lymphovenous Centre, Herestraat 49, B-3000 Leuven, Belgium
25 (nele.devoogdt@uzleuven.be)
- 26 6. Antwerp University Hospital, department of thorax and vascular surgery, Wilrijkstraat 10,
27 2650 Edegem, Belgium (e-mail: lore.fias@uza.be)
- 28 7. Antwerp University Hospital, Multidisciplinary breast clinic, Wilrijkstraat 10, 2650 Edegem,
29 Belgium (e-mail: wiebren.tjalma@uza.be)

30 Corresponding author:

31 Prof. dr. Nick Gebruers

32 Department of Rehabilitation Sciences and Physiotherapy; MOVANT research group; Faculty of
33 Medicine and Health Sciences

34 University of Antwerp

35 Universiteitsplein 1

36 2610 Antwerp (Belgium)

37 nick.gebruers@uantwerpen.be

38 Tel: +32 3 265 2876

39 Fax: +32 3 265 2501

1 In response to the comments made by Sun et al. concerning the use of prediction formulas¹ as
2 mentioned in our practice guideline². On the one hand, we like to stress that pre-operative
3 measurements of patients undergoing treatment for breast cancer is a very good approach to monitor
4 (lymph)edema formation afterwards³; taking into account that a comparison to the non-affected arm
5 is always included and not solely a comparison to pre-operative values is being assessed. However, in
6 current practice, these pre-operative volumes are mostly (> 95% of the cases in Belgium) lacking.
7 Therefore keeping in mind, that it was our goal to write a best practice guideline, an alternative
8 approach had to be discussed; being the use of prediction formulas.

9 On the other hand, we do believe that prediction formulas have a clinical relevance in daily practice.
10 We have several arguments to motivate this statement. **First**, several studies concerning the treatment
11 of breast cancer related lymphedema (BCRL) have found reductions of the edema volume that exceed
12 100%⁴; meaning that a correction of the volume would have been useful. In these type of studies the
13 real edema volume is underestimated. **Second**, in some countries, the amount of difference between
14 both arms is related to the amount of reimbursement of the treatment. Therefore, not correcting the
15 volume of the non-dominant arm; yet the lymphedematous arm; would sometimes result in reduced
16 reimbursement since the total edema volume is misinterpret by at least 3.3% . **Third**, we believe that
17 using perometry in combination with the prediction formulas is not the most sensitive way to perform
18 edema calculations⁵. Although perometry has been found valid and reliable⁵; we doubt the sensitivity
19 in comparison to a water displacement method as described by Gebruers et al¹. From our own
20 measurements performed with perometry (data not yet published), we have found that the variance
21 on repeated test- retest measures (with strict standardization of the measurement procedure) is
22 between 2.68% and 3.85% in BCRL-patients. In comparison, the water displacement method used to
23 determine the prediction formulas has a variance of 0.63% for test- retest repeated measures in
24 patients. Therefore a water displacement method (golden standard) is more sensitive than perometry
25 and cannot be used interchangeable with the prediction formulas. **Fourth**, wide limits of agreement
26 (LOA) have been demonstrated among several different tools to assess lymphedema despite excellent

1 correlations between the different protocols. Therefore wide LOA only demonstrate that different
2 protocols should not be used interchangeably⁶. **Fifth**, the prediction formulas have been used in the
3 EforT-BCRL trial (<https://clinicaltrials.gov/ct2/show/NCT02609724>) a RCT comparing three different
4 types of manual lymphatic drainage in patients with BCRL⁷. One of the inclusion criteria is “ at least 5%
5 volume difference between affected and non-affected arm”. To determine this difference, the
6 prediction formulas are used during the intake. Afterwards these findings are confirmed (cross
7 validated) by a lymphofluoroscopy⁸; so far, demonstrating a defect in the lymphatic architecture in all
8 of the included patients (n=140).

9 To conclude; we strongly agree with the use of pre-operative arm volumes to monitor lymphedema
10 formation when available. Until preoperative measurements have become common practice; the use
11 of prediction formulas are a clinically relevant alternative when a water displacement method is used.

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1 References

- 2 1. Gebruers N, Truijen S, Engelborghs S, De Deyn PP. Volumetric evaluation of upper extremities
3 in 250 healthy persons. *Clin Physiol Funct Imaging* 2007;27:17-22.
- 4 2. Gebruers N, Verbelen H, De Vrieze T, Vos L, Devoogdt N, Fias L, et al. Current and future
5 perspectives on the evaluation, prevention and conservative management of breast cancer related
6 lymphoedema: A best practice guideline. *Eur J Obstet Gynecol Reprod Biol* 2017;216:245-53.
- 7 3. Sun F, Skolny MN, Swaroop MN, Rawal B, Catalano PJ, Brunelle CL, et al. The need for
8 preoperative baseline arm measurement to accurately quantify breast cancer-related lymphedema.
9 *Breast Cancer Res Treat* 2016;157:229-40.
- 10 4. Szuba A, Cooke JP, Yousuf S, Rockson SG. Decongestive lymphatic therapy for patients with
11 cancer-related or primary lymphedema. *Am J Med* 2000;109:296-300.
- 12 5. Hidding JT, Viehoff PB, Beurskens CH, van Laarhoven HW, Nijhuis-van der Sanden MW, van
13 der Wees PJ. Measurement Properties of Instruments for Measuring of Lymphedema: Systematic
14 Review. *Phys Ther* 2016;96:1965-81.
- 15 6. Batista BN, Baiocchi JMT, Campanholi LL, Bergmann A, Duprat JP. Agreement between
16 Perometry and Sequential Arm Circumference Measurements in Objective Determination of Arm
17 Volume. *J Reconstr Microsurg* 2018;34:29-34.
- 18 7. De Vrieze T, Vos L, Gebruers N, Tjalma WAA, Thomis S, Neven P, et al. Protocol of a
19 randomised controlled trial regarding the effectiveness of fluoroscopy-guided manual lymph
20 drainage for the treatment of breast cancer-related lymphoedema (EforT-BCRL trial). *Eur J Obstet*
21 *Gynecol Reprod Biol* 2018;221:177-88.
- 22 8. Belgrado JP, Vandermeeren L, Vankerckhove S, Valsamis JB, Malloizel-Delaunay J, Moraine JJ,
23 et al. Near-Infrared Fluorescence Lymphatic Imaging to Reconsider Occlusion Pressure of Superficial
24 Lymphatic Collectors in Upper Extremities of Healthy Volunteers. *Lymphat Res Biol* 2016.

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