Can manual lymph drainage be improved or not : thats the question! A response letter

Dear Editor in Chief,

With interest we have read the comments stated by prof. dr. Bourgeois regarding the recently published protocol of the EFforT-BCRL trial[1]. However, the mentioned 'concerns' cited in this letter are unjustified in our opinion. For this reason, we would like to provide some clarification on the basis of following response letter.

First, following statement is made: *"Their 'traditional' MLD (in their group B) seems to be what they do themselves but, neither what many other Belgian physiotherapists do routinely, nor what is done in other countries. Indeed, they write that manoeuvers "to create resorption of lymph" are part of their "new" MLD but are not mentioned when they describe what they define as "traditional" MLD. Unfortunately for the authors, these manoeuvers are part of the MLD for instance taught by the Foeldi's and Leduc's schools. Thus, the conclusions of their study could not be used to omit MLD taught by these schools."*

It is correct that there are multiple schools educating MLD (e.g. Lerhner, Casley-Smith, Leduc, Vodder, and colleagues) and despite these are different methods, they all have common characteristics as well. For example, one important aspect in this is the fact that in all cases MLD is being applied with the assumption that every patient has a ~~normal lymphatic anatomy~~lymphatic architecture as a 'healthy' subject. In other words, MLD is being applied blindly, without knowledge of the patient-specific superficial lymphatic network. In light of this, the added values of fluoroscopy-guided MLD are the knowledge about this patient-specific anatomy due to the fluoroscopy, as well as the altered hand maneuvers. The fact that many Belgian therapists routinely do something different, is in our opinion rather a weakness in Belgium. For this reason, as well as to eliminate all subjective feelings about MLD, the conduction of a multicenter, double-blinded and standardized randomized controlled trial (RCT) is required.

Furthermore, a consensus regarding the 'traditional' MLD method was reached~~: 1)~~ after discussion with a team of experts in the field of lymphology with manifold years of experience in MLD method Leduc~~'s~~ and MLD method Vodder. The additional effect of these two methods has already been investigated in different RCTs. The meta-analyses of Huang and Cochrane systematic review of Ezzo concluded that the additional effect of MLD is rather limited. We would investigate whether a more efficient method of MLD is more effective that the previously investigated methods of MLD (= traditional MLD). ~~'s MLD techniques, and 2) based on the (limited) amount of evidence concerning these techniques that is currently available in literature. In the meta-analysis of Huang et al, in which the effects of MLD in the treatment of breast cancer-related lymphoedema were questioned, the different applied MLD methods in the 6 included RCT's, were massed together[2]. Accordingly, we entitled this group 'traditional MLD', which is in line with the applied MLD in our study.~~

Second, the value of the future conclusions resulting from this trial is questioned because of following statement: *"if results would reveal that the fluoroscopy-guided MLD yields a better outcome compared to the traditional MLD and/or the placebo MLD, one does still not know whether this is due to the knowledge of the patient-specific lymphatic anatomy, or due to the altered MLD maneuvers"*.

In our opinion, it is incorrect stating that the protocol will not allow any valuable conclusion. The aim of our study is to investigate the effect of a completely optimized MLD technique (i.e. optimization of the MLD maneuvers of which physiological effects after one session of fluoroscopy-guided MLD have

Met opmerkingen [GN1]: Ik zou je antwoord ook een titel geven: bvb

The Effort-trial is a well-constructed RCT! A response letter Can MLD be improved or not, that's the question! A response letter

Op deze manier wordt je brief beter zoekbaar in de databanken

Met opmerkingen [GN2]: Een optie is om hier nog heel even het doel van de effort te herhalen en vervolgens te stellen dat het protocol geschreven is door alle stakeholders en volgens het CONSORT/SPIRIT richtlijnen om te voldoen aan alle kwliteitsnormen van een RCT

Met opmerkingen [TDV3]: Mag je de naam noemen indien er geen 'et al' bij komt? Refereren ernaar kan nog niet

Met opmerkingen [GN4]: Ik zie dat Nele het te aanvallend vind. Echter hij heft de brief geschreven en je verwijst naar zijn schrijven. Tevens zullen beide brieven na elkaar gepubliceerd worden, iedreen weet toch waarop je reageert.

Voor mij is het dus gelijk hoe je het verwoord

Met opmerkingen [ND5]: Ik zou dit verwijderen. Is te aanvallend.

Met opmerkingen [ND6]: Kan je de 'common characteristics' benoemen?
In 1998 zijn er 4 artikels verschenen over MLD method Casley-Smith, Leduc, Lerner en Vodder (van Kasseroller). Anders deze eens opzoeken?

Dit weglaten. Zijn opmerking gaat over de handgrepen, die verschillend zijn tussen de verschillende methodes.
Dat van kinesitherapeuten in België zou ik weglaten: zo bekritiseer je de kine in België en eigenlijk weten we dat niet en we weten ook niet wat het belang daarvan is.

already been proven[3,4], and having knowledge of the patient-specific lymphatic network). In case this technique shows to be more effective, a new study ~~can~~ has to be set up to investigate why it is more effective: because of the maneuvers or because of the knowledge of the lymphatic network. Additionally, given the fact that the more recently published RCT's investigating the added value of MLD, failed to prove an additional effect[5,6], and a Cochrane systematic review only showed an additional effect of 7%[7], there is a valid reason to question this added value and to further investigate it. Therefore, we found it important to also have the ability to compare results with a group receiving a placebo MLD, in order to investigate whether MLD has an additional effect or not.

Third, four rather unspecified tricky points were named to end with.

- It is mentioned that we are *"using multi-layer bandaging with component different from the one used by other physiotherapists"* as cited in the comment; however, we are applying this type of multi-layer bandaging as a standard treatment since it is based on the available evidence found in literature. Additionally, this method of bandaging is recommended by the International Compression Club (ICC), as it is also the applied technique in the 3 expertise centers in Belgium (UMC St-Pierre University Hospital Brussels, University Hospitals Leuven, and CHU UCL Godinne University Hospital Namur). Nevertheless, in case of any scientific evidence against the use of technique, we would be thrilled to learn from it. Unfortunately, we were unable to find any supporting references of RCT's recommending the use of a certain technique over another.
- It is correct that the two physiotherapists LV and TDV are not known as being working in the department of rehabilitation of the St Pierre University Hospital, nor in one of the other participating centers. However, both therapists are specialised in the field of lymphology and consequently also in the decongestive lymphatic therapy. For this reason, and based on the approval by the Ethical Committee of the University Hospitals of Leuven (main Ethical Committee) and the received positive advise from the Ethical Committees of all other participating centres (CME reference S58689, EudraCT Number 2015-004822-33), both therapists carry out the treatments in all study centres.
- The reason why *"the use of specific systems for the volumetric and perimetric evaluations"* is mentioned as a tricky point is not entirely clear to us; unfortunately, the reason why such a statement is made, is lacking. Reliability of circumference measurements using a perimeter has been proven[8], and investigation regarding reliability of the applied water displacement method in the EFforT- BCRL trial has been conducted and is in preparation[9] + De Vrieze et al.
- The reproducibility of the lymphofluoroscopic investigations is unknown, which is true. Nevertheless, reproducibility is only a problem if one aims to make firm conclusions based on images in relation to time. In order to work out the patient-specific fluoroscopy-guided MLD strategy with different hand maneuvers applied on different regions, schemes are based on findings resulted from the baseline fluoroscopy. The fact that a certain lymph collector is not being visualized during a second fluoroscopy on a later moment in time, is in our opinion still less worse than working completely blindly. However, reproducibility of the fluoroscopic investigations is also being investigated in current trial, with the aim to provide an evidence-based answer to this important question in due course.

That being said, we hope to have offered elucidating answers to the concerns that may have been arisen.

Met opmerkingen [GN7]: Je kan buiten het eigen artikel dat nog in voorbereiding is; ook de refs van andere volumetrie systemen toeveogen en een algemen boodschap weergeven dat volumetrie geld al seen gouden standard en valide en betrouwbaar is, dank an je DAmstra, mezelf en andere refereren.

Met opmerkingen [TDV8]: Of hoe doe je dit; moet ik een aparte referentie maken met enkel auteur en titel of?

Met opmerkingen [ND9R8]: Ik zou schrijven:
Reliability of circumference measurements using a perimeter has been proven[8], and reliability of the applied water displacement method to determine the arm and hand volume as well (hier gewoon nummer achter plaatsen)

Je referentie is dan: De Vrieze, co-auteurs van je artikel ertussen, Devoogdt. Titel artikel. In publication.

Met opmerkingen [TDV10]: Is volledig waar, maar kan het dan geen kwaad dat onze 'vooringenomen' hypothese zo een beetje duidelijk wordt? Of maakt dan niet zozeer uit?

Met opmerkingen [ND11]: The lymphofluoroscopic investigations are used to determine the patient specific superficial lymphatic architecture. The authors will further investigate reproducibility of this imaging technique (in the same way they have investigated reproducibility of the lymphoscintigraphy in 2014).

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3. Belgrado JP, Vandermeeren L, Vankerckhove S, et al. Near-Infrared Fluorescence Lymphatic Imaging to Reconsider Occlusion Pressure of Superficial Lymphatic Collectors in Upper Extremities of Healthy Volunteers. Lymphat Res Biol 2016;**14**(2):70-7 doi: 10.1089/lrb.2015.0040[published Online First: Epub Date]|.
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6. Gradalski T, Ochalek K, Kurpiewska J. Complex Decongestive Lymphatic Therapy With or Without Vodder II Manual Lymph Drainage in More Severe Chronic Postmastectomy Upper Limb Lymphedema: A Randomized Noninferiority Prospective Study. Journal of pain and symptom management 2015;**50**(6):750-7 doi: 10.1016/j.jpainsymman.2015.06.017[published Online First: Epub Date]|.
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9. Evaluation of the reliability of four measuring methods of hand's perimeter and volume: Buoyancy Forces Valgrado System, circumference measurement, figure-of-eight method and Manu3Metrix scanner. 8th International Lymphoedema Framework Conference; 2018; Rotterdam, The Netherlands.