



CORRESPONDENCE

Comment on: ‘Increases in arm volume predict lymphoedema and quality of life deficits after axillary surgery: a prospective cohort study.’

British Journal of Cancer (2021) 124:1606–1607; <https://doi.org/10.1038/s41416-021-01267-3>

We commend Bundred et al. for completing their multicentre prospective study but, their claim that “bioimpedance spectroscopy (BIS) alone is not appropriate for lymphoedema screening or diagnosis”, does not fit with screening principles or current evidence, nor does their data support this conclusion.¹

All patients underwent an axillary dissection and prescribed a compression garment when diagnosed with breast cancer-related lymphedema (BCRL), defined as perometry-based relative arm volume increase (RAVI) of >10%. This self-defined “gold-standard” was compared to other measures including bioimpedance spectroscopy (BIS) of >7.5 or ≥ 10 L-Dex units. BCRL (RAVI > 10%) was 22.4% at 24 months as compared with 45.2% for BIS ≥ 10 or 57.6% for BIS > 7.5.

We have several concerns with the study methods and conclusions. First, the study compares clinical lymphoedema (RAVI > 10%) to BIS, but the authors, in their introduction, noted a RAVI ≥ 5% as more suitable for early intervention. When this lower threshold was used, 51.4% met this criterion that closely correlated with BIS and symptoms (Fig. 1). Early intervention is best implemented when there is subclinical BCRL (sBCRL) before adipose differentiation, and subsequent fibrosis occurs.

Early detection of BIS changes and timely intervention with complex decongestive physiotherapy (CDP) is thought to reduce clinical progression.² As clinicians treating breast cancer and contributing to BCRL, we have used BIS with over 35 years of collective experience and recognise its simplicity, reproducibility and patient acceptability.³ Waiting for clinical BCRL to develop, then prescribing a compression garment, is as inappropriate as waiting for breast cancer to become clinically palpable, rather than detecting it when not palpable with better outcomes.

In contrast to the authors’ conclusions, previous studies have found that BIS is an objective measure for patients with sBCRL (>6.5). Early intervention with non-invasive measures (including skin care, self-massage and a 23–32 mm compression garment) are less intensive and less costly than CDP.⁴ BIS, particularly when performed using newer upright scale-like devices, provides immediate feedback and can be done quickly by any trained staff in several minutes.⁵ It has been used in Australia for 15-years and relatively easy to implement into clinical practice. Measuring girth when fat and fibrosis has set in is not the aim of L-Dex (or prospective surveillance) and not good clinical practice. The principle of early detection is to diagnose sBCRL which correlates with patients’ symptoms (suggesting an already developing pathologic condition) and, intervene with compression at that stage, which appears to assist reversal of the condition as demonstrated by ICG studies.⁶

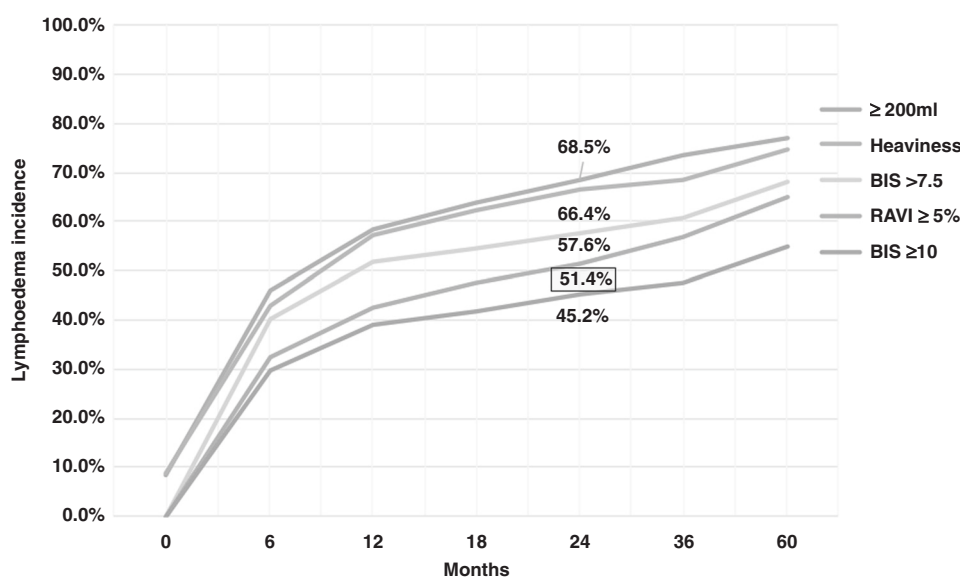


Fig. 1 Probability of lymphoedema defined by the various volume or bioimpedance measures (derived from ref. ¹). Highlighted percentage is the 24-month incidence of lymphoedema defined as a relative arm volume increase (RAVI) of ≥5%. BIS = bioimpedance spectroscopy (BIS) L-Dex units.

Received: 4 July 2020 Revised: 15 September 2020 Accepted: 2 October 2020
Published online: 2 February 2021

A second concern is the study's claim that a measure at 6-months predicts outcomes at 24 months, is difficult to justify when only 49.5% of patients were evaluable at 24 months, 28.5% at 36 months and 14.2% at 60 months which the authors attribute to the "anxiety-provoking" experience of coming to clinic. Our experience shows that regular BIS L-Dex checks can be done in radiotherapy, medical oncology, specimen collection laboratories or "lymphoedema departments" with excellent attendance rates⁷. We similarly do not stop checking follow-up mammograms based on this logic.

Finally, we are perplexed by the high rates of BIS increases and lower rates for RAVI. Ridner (2019) evaluated triggering rates for potential sBCRL by randomly comparing BIS (L-Dex ≥ 6.5) versus TM-derived RAVI $> 5\%$ and found that BIS had a lower rate (BIS:15.8% versus TM: 28.5%, $p < 0.001$) and longer times to trigger (BIS: 9.5 vs. TM 2.8 months, $p = 0.002$). BIS also reduced the absolute rates of progression of clinical BCRL requiring CDP by approximately 10% (TM: 14.7%, BIS: 4.9%), a clinically relevant improvement.⁸ This discrepancy may reflect the difference between perometry measures which can vary by arm position, the use of RAVI $> 5\%$ rather than 10%, the strict protocol conditions and the more complete follow-up in the Ridner study.⁹

Although the authors argue that the gold standard is RAVI $\geq 10\%$, we firmly believe that this is too late in the disease development for intervention to make a meaningful difference. The use of BIS together with TM as required is a cost-effective, patient-centred approach with the added advantage of measuring body composition so commonly affected by weight gain or chemotherapy-induced sarcopenia. Importantly, RAVI $> 5\%$ (i.e. subclinical BCRL) is highly correlated with L-Dex and the incidence at 24 months (51.4%), is midway between BIS ≥ 10 (45.2%) and BIS > 7.5 (57.6%) (Fig. 1).

L-Dex is convenient and less anxiety-provoking than perometry, which is a larger prohibitively expensive device, more efficient than TM-derived volume differences and can be implemented with information and psychological support to improve adherence to best-practice care.¹⁰

ACKNOWLEDGEMENTS

Not applicable.

AUTHOR CONTRIBUTIONS

J.B. conceived the correspondence and wrote the first draft. S.S. and F.V. actively critically reviewed the manuscript. All authors approved the final version.

ADDITIONAL INFORMATION

Ethics approval and consent to participate Not applicable.

Consent to publish Not applicable.


Data availability Not applicable.

Competing interests J. Boyages-stockholder ImpediMed Limited, F.A. Vicini-Chief Medical Officer, ImpediMed Inc, C. Shah- Consultant—ImpediMed Inc, Grants—Varian Medical Systems, VisionRT, PreludeDX. ImpediMed Ltd. had no involvement in the conception or writing of this Correspondence.

Funding information Not applicable.

Note This work is published under the standard license to publish agreement. After 12 months the work will become freely available and the license terms will switch to a Creative Commons Attribution 4.0 International (CC BY 4.0).

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

John Boyages ¹, Chirag Shah² and Frank A. Vicini³
¹Icon Cancer Centre, Wahroonga, NSW, Australia; ²Cleveland Clinic, Taussig Cancer Institute, Department of Radiation Oncology, Cleveland, OH, USA and ³21st Century Oncology, Michigan Healthcare Professionals, Farmington Hills, MI, USA
 Correspondence: John Boyages (john.boyages@icon.team)

REFERENCES

- Bundred, N., Foden, P., Todd, C., Morris, J., Watterson, D., Purushotham, A. et al. Increases in arm volume predict lymphoedema and quality of life deficits after axillary surgery: a prospective cohort study. *Br. J. Cancer* **123**, 17–25 (2020).
- Network, N. C. C. *NCCN Clinical Practice Guidelines in Oncology*, Accessed 30/06/2020 (2020).
- Koelmeyer, L. A., Borotkanics, R. J., Alcorso, J., Prah, P., Winch, C. J., Nakhel, K. et al. Early surveillance is associated with less incidence and severity of breast cancer-related lymphedema compared with a traditional referral model of care. *Cancer* **125**, 854–862 (2019).
- Stout Gergich, N. L., Pfalzer, L. A., McGarvey, C., Springer, B., Gerber, L. H. & Soballe, P. Preoperative assessment enables the early diagnosis and successful treatment of lymphedema. *Cancer* **112**, 2809–2819 (2008).
- Koelmeyer, L. A., Ward, L. C., Dean, C. & Boyages, J. Body positional effects on bioimpedance spectroscopy measurements for lymphedema assessment of the Arm. *Lymphat. Res. Biol.* **18**, 464–473 (2020).
- Akita, S., Nakamura, R., Yamamoto, N., Tokumoto, H., Ishigaki, T., Yamaji, Y. et al. Early detection of lymphatic disorder and treatment for lymphedema following breast cancer. *Plast. Reconstr. surgery* **138**, 192e–202e (2016).
- Koelmeyer, L., Gaitatzis, K., Ridner, S. H., Boyages, J., Nelms, J., Hughes, T. M. et al. Implementing a prospective surveillance and early intervention model of care for breast cancer-related lymphedema into clinical practice: application of the RE-AIM framework. *Support. Care Cancer*, **29**, 1081–1089 (2020).
- Ridner, S. H., Dietrich, M. S., Cowher, M. S., Taback, B., McLaughlin, S., Ajkay, N. et al. A Randomized trial evaluating bioimpedance spectroscopy versus tape measurement for the prevention of lymphedema following treatment for breast cancer: interim analysis. *Ann. Surg. Oncol.* <https://doi.org/10.1245/s10434-019-07344-5> (2019).
- Stanton, A., Northfield, J., Holroyd, B., Mortimer, P. & Levick, J. Validation of an optoelectronic limb volumeter (Perometer®). *Lymphology* **30**, 77–97 (1997).
- Sherman, K. A. & Koelmeyer, L. Psychosocial predictors of adherence to lymphedema risk minimization guidelines among women with breast cancer. *Psycho-Oncology* **22**, 1120–1126 (2013).