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Response to: Gschwantler-Kaulich et al (2016) Mesh versus acellular dermal matrix in immediate implant-based breast reconstruction – A prospective randomized trial

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Dear Professor Audisio,

We read with great interest the recent pilot randomised controlled trial (RCT) comparing biological and synthetic meshes in implant-based breast reconstruction (IBBR)[1].

We agree that RCTs in this field are needed but have concerns about this study. Primarily, we would question whether this is indeed a 'pilot study'. Pilot studies aim to test the feasibility, reliability and validity of the proposed design of a main RCT[3]. They may aim to determine, for example, whether it is possible to recruit and randomise patients or explore the best primary endpoint for the main trial. They may also test whether the components of the main study can work together[4]. Published reports should be largely descriptive and provide important methodological information such as the standard deviation of the primary end-point to inform a sample-size calculation. They should not include hypothesis-testing as any estimate the effect-size would be very imprecise and potentially misleading[5]. We would suggest that, rather than a pilot study, this study is a small trial that is insufficiently well-designed to look at the target differences between treatment groups. There are, however, some useful design features that can be gleaned from the report that could be used to inform a definitive trial.

Firstly, although the numbers of patients eligible and the numbers approached to participate in the study are not reported, 50 patients from four centres were randomised over the 11-month study-period and of these, 48 received their allocated treatment. This suggests that randomisation may be acceptable to both patients and surgeons and that a multicentre large RCT may be feasible. Although the study did not present a primary end-point or consider what this should be a main trial, it did show that data could be collected on a range of outcomes including cosmesis, complications, patient satisfaction and quality of life. Complications, however, were not defined and although validated patient-reported outcome measures

(EORTC-C30 and BR-23) were used, these are not specific or sufficiently sensitive for use in the study population[6]. The main study will require carefully-selected end-points and inclusion of the recently-developed core outcome set for breast reconstruction[7] will ensure that key outcomes of importance to both patients and healthcare professionals are evaluated. Finally, it was unclear why Protexa was selected as the comparator biological mesh and whether this could be used in multiple international centres in a main trial as this product is not widely-used, particularly in the UK.

The iBRA (implant Breast Reconstruction evAluation) study (ISRCTN37664281) is an on-going prospective multicentre cohort study which aims to inform the feasibility, design and conduct of an RCT in IBBR. It will define current practice and explore issues surrounding recruitment; selection of comparators; choice of primary outcome; sample-size and selection criteria using a trainee collaborative approach[8]. It is hoped that the iBRA study will lead to a definitive large-scale RCT in IBBR that reflects current practice and furthermore will create network of research-active trainees and consultants engaged in the need for evaluation who will be willing and able to participate in and deliver the future trial.

Shelley Potter

Chris Holcombe

Jane Blazeby

On behalf of the iBRA Research Collaborative

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