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Reponse to: comment on, 'Tumour-stroma ratio (TSR) in oestrogen-positive breast cancer patients'

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Sir,

We thank Dr Mesker *et al* for their comments on our study, (Downey *et al*, 2014) recognising their significant work promoting the concept of using tumour-stroma ratio (TSR) to determine the outcome in cancer (Mesker *et al*, 2007, 2009; Courrech Stall *et al*, 2010, 2011; de Kruijf *et al*, 2011; Dekker *et al*, 2013; Huijbers *et al*, 2013).

None of our ER-positive cohort (118 female, 62 males; Downey *et al*, 2014) received neoadjuvant therapy of any type. Neoadjuvant treatment induces pathological changes in the tumour, hence would render samples unsuitable for TSR analysis. We were limited in the amount of information that could be supplied in a short communication, however univariate and multivariate outcomes were provided.

We found high stromal content was related to better survival across genders in ER-positive disease (Downey *et al*, 2014), contrasting data in triple-negative breast cancer (de Kruijf *et al*, 2011) and, as highlighted by Mesker *et al*, their own work on ER-positive cases (de Kruijf *et al*, 2011; Dekker *et al*, 2013). As breast cancer is heterogeneous, subtle differences in stromal biology may exist between breast cancer subtypes, potentially impacting on outcome. Notably, tubular carcinoma, a type of invasive breast ductal carcinoma with an abundant stroma (Figure 1), is almost always ER-positive and has a favourable prognosis (Rakha *et al*, 2010).

Methodological heterogeneity exists between sampling methods used to assess TSR. Two key issues stand out: (1) lack of standardisation in TSR measurement, (2) area of tissue selected for analysis. Our in-house computer algorithm method selects a 9 mm^2 area of a digitally scanned H&E image (Downey *et al*, 2014). Recent related work assessed TSR manually in a single section from the most invasive tumour area (Gujam *et al*, 2014). Mesker *et al* favour assessment of the whole slide, even suggesting an evaluation of all available microscope slides. Although rigorous assessment is to be commended, this technique may have practical implications for histopathologists should TSR evaluation ever become routine. Alternative approaches should be considered, compared and validated.

We believe that there is much more to the stroma in dictating outcome, than simply its proportion in relation to tumour. There is a need to examine the cell types that coexist within tumour stroma, for example, fibroblasts and immune cells (Hanahan and Coussens, 2012); a recent issue of this journal showed that patients with a high TSR had significantly reduced inflammatory cell infiltrate within their stroma (Gujam *et al*, 2014). It remains possible that discrepancies observed between studies of TSR in breast cancer may be due in part to components of the stromal microenvironment.

Consistent with all emerging techniques it takes time for the ideal methodology to become accepted in the field. We respectfully suggest the best way to achieve this for TSR is through collaboration, comparing different techniques, using carefully selected sub groups of breast cancer and working towards reaching a consensus, taking account not only of the stroma but the cells within.
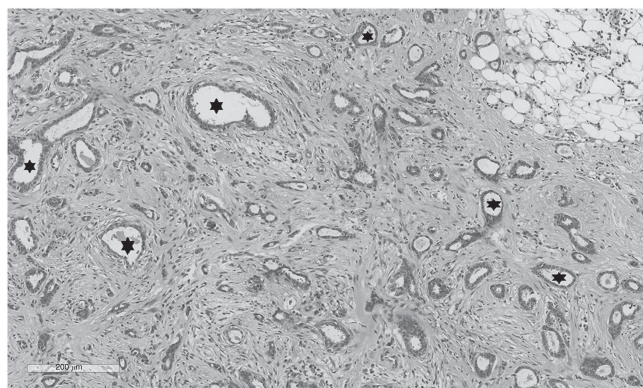

Figure 1. Tubular carcinoma showing arrangement of tumour cells in characteristic tubes (stars) embedded within an abundant multicellular stroma. Scale bar = 200 µm.

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BJC

Comment on 'Reasons for non-uptake and subsequent participation in the NHS bowel cancer screening programme: a qualitative study'

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Sir,

We read this paper by Palmer *et al* (2014) regarding participation in the Bowel Cancer Screening Programme (BCSP) with great interest. At the time of publication we had developed pilot screening education sessions in South London. By running the programme as a group of health care professionals (HCPs) consisting of junior doctors, and in partnership with Bowel Cancer UK, we would assess whether such HCP endorsement improved screening uptake.

South London area has low screening uptake (unpublished data), and consists of many communities of socio-economically deprived and ethnic minority populations. Indeed, previous studies show that such groups correlate with poor screening uptake (Von Wagner *et al*, 2011; Lo *et al*, 2014). Bowel Cancer UK has links with these community groups, some of whom invited us to speak, advertising internally to bring our audience. In our pilot phase, sessions have only been one off, but we anticipate returning annually if not more frequently, for new participants as well as to maintain bowel cancer and screening awareness. Education sessions were informal and held at the convenience of participating groups, via a standardised presentation. Participants were given information regarding the epidemiology and risk factors for bowel cancer. In particular, we covered the importance of screening asymptomatic individuals and performed a demonstration and thorough explanation of the faecal occult blood (FOB) test. Participants were encouraged to ask questions before, during and after the presentation, and were sometimes quizzed during the sessions to enable an educational experience that was both informative and enjoyable. Feedback using a Likert scale on how useful the sessions were showed that every participant found the presentation very useful (85.7%) or quite useful (14.3%).

In our pilot study, we were invited to deliver talks to 43 participants from three community groups—users of the local library, the local Chinese association and the local Irish pensioners association. Our talks were attended disproportionately by women (male: 13; female: 30) due to the variation in participation in these local community groups. For the same reason, our sessions were attended by individuals from a wide range of ages although the majority were aged between 50 and 69 (53.4%). We did not distinguish between younger (screening naive) and older (screening age) groups in the hope of positively influencing the decision to participate in screening when invited in future in the former group, and consolidating the knowledge and FOB testing know-how in the latter group.

A large proportion of our participants (51%) were of ethnic minority origin and sometimes interpreters were required for the talks. This is important as screening uptake in ethnic minorities could be poor secondary to the language barrier. This draws attention to the potential influence of discussion to ethnically diverse groups, as Palmer *et al* held focus groups comprising mostly white Europeans.

Prior to the education sessions, 63.2% of participants reported awareness of the screening programme with 41.5% reporting that they would take part. Their willingness to participate in the screening programme improved to 85.7% after the talk. Before the session, only 27.9% were aware of the symptoms associated with bowel cancer. This improved to 92.8% after the talks. Furthermore, 92.8% reported that they would see their GP if they were to experience any symptoms associated with bowel cancer. Moreover, 82.1% felt more comfortable talking about bowel cancer and the screening programme with friends and family. This increased willingness to participate in the screening programme after the educational programme draws parallels to the findings by Palmer *et al*, after their participants had the opportunity to discuss screening with others. However, despite the improvement in the understanding of bowel cancer and risk factors, only 23–50% expressed willingness to make lifestyle changes such as smoking cessation. Annual sessions would serve as follow-up to assess whether participants actually took part in screening after an educational session.

Although our pilot study looked at a very small number of participants, our results have been consistent with the qualitative data collected by Palmer *et al* in showing the benefits of discussion to dispel misconceptions and also to encourage and support participation in the screening programme. Palmer *et al* reported that many participants claimed they were more likely to participate in FOB testing if it were endorsed by HCPs. Further research with larger groups of people may prove to be beneficial in assessing whether running wide-scale HCP-endorsed bowel cancer screening is cost-effective to bring long-term improvement to the uptake of bowel cancer screening.

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