Enhanced biological effectiveness of low energy X-rays and implications for the UK breast screening programme

The Editor—Sir,

A recent paper by Heyes et al published in the *British Journal of Radiology* [1] discusses the potential carcinogenic side effects of screening mammography, a topic of great public interest, concern and importance. Based in particular on their earlier report comparing dose responses of mammography X-rays and higher energy beta and gamma radiations for the endpoint of neoplastic transformation [2], the authors conclude that ''low energy X-rays as used in mammography are approximately four times – but possibly as much as six times – more effective in causing mutational damage than higher energy X-rays.'' They further conclude that ''…this implies that the risks of radiation-induced breast cancers for mammography X-rays are underestimated by the same factor.''

Unfortunately, the authors' risk estimation is based on high dose data, with a linear extrapolation to low doses. The lowest dose in the mammography X-ray data used by the authors for their extrapolation was 270 mGy, *i.e.* approximately 100 times higher than the dose experienced in screening mammography [3]. Similarly, the lowest dose of high-energy, low LET radiation used for the comparison of effects was 1 Gy [2]. Even more unfortunately, the authors fail to cite and discuss several papers using the same endpoint as that of the authors', showing that the dose–response curves for both high and low energy low LET radiations do not adhere to a linear extrapolation at low doses (<100 mGy) and demonstrating that extrapolation from higher doses is likely to significantly overestimate the risk [4–9]. Indeed, at such low doses of a variety of low LET radiations there is reproducible evidence for a suppression of transformation frequency below background levels, *i.e.* a J-shaped dose–response curve [6]. This type of response implies that the doses used in mammography screening may reduce, rather than increase breast cancer risk. In particular, the authors fail to discuss a paper, using the same cell assay system and the same mammographic energy X-rays, that reported the effect of doses as low as 0.54 mGy (*i.e.* in the range of screening mammography examinations) and up to 220 mGy, and which also showed a clear J-shaped dose–response curve [9]. The data from that latter paper, when normalized for background levels of neoplastic transformation, fit well with the original data of Heyes and Mill [2] upon which their current article is based (Figure 1), again clearly illustrating that linear extrapolation overestimates risk for neoplastic transformation at the doses used in mammography. Furthermore, epidemiological studies of breast cancer induction by a variety of low-LET radiations

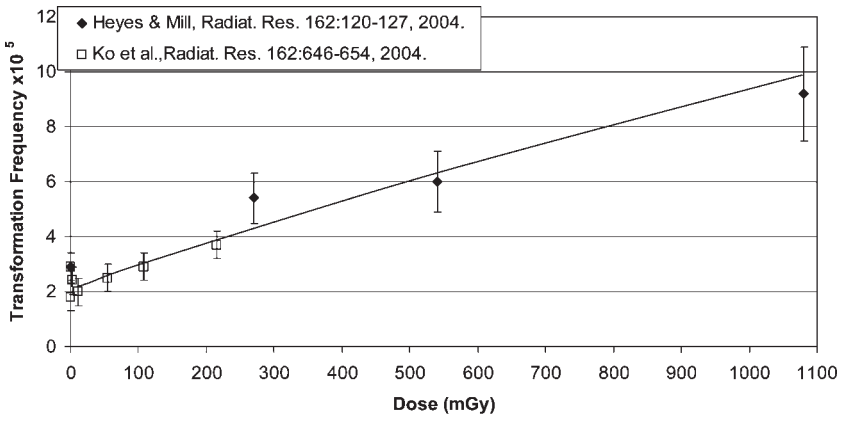

Figure 1. Transformation frequency as a function of dose of mammographic energy X-rays: a comparison of two data sets normalized to the spontaneous frequency in Heyes and Mill, 2004 [2].

show no evidence for significant breast cancer induction at doses < 100 mGy [10]. In addition, a very recently published case-control study also found no that evidence for screening mammography contributes to the burden of breast cancer in high risk women carrying the BRCA1 or BRCA2 mutation [11].

The question of the shape of the dose–response curve at low doses, and hence the estimation of radiation risks at low doses, continues to be a subject of controversy, as is witnessed by the opposing conclusions of the US National Academy of Sciences BEIR VII Phase 2 report and those of the French Academies of Medicine and Science [12, 13]. It is, therefore, particularly important that all published data relevant to this topic be cited, and fully and objectively discussed. On a topic of great public interest and societal importance, Heyes et al [1] have failed to do this and in that failing have done a disservice to the readership.

Yours etc.,

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