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Research article

Mathematical modelling of radiation-induced cancer risk from breast screening by mammography

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ABSTRACT

Objectives: Establish a method to determine and convey lifetime radiation risk from FFDM screening.
Methods: Radiation risk from screening mammography was quantified using effective risk (number of radiation-induced cancer cases/million). For effective risk calculations, organ doses and examined breast MGD were used. Screening mammography was simulated by exposing a breast phantom for cranio-caudal and medio-lateral oblique for each breast using 16 FFDM machines. An ATOM phantom loaded with TLD dosimeters was positioned in contact with the breast phantom to simulate the client's body. Effective risk data were analysed using SPSS software to establish a regression model to predict the effective risk of any screening programme. Graphs were generated to extrapolate the effective risk of all screening programmes for a range of commencement ages and time intervals between screens.
Results: The most important parameters controlling clients' total effective risk within breast screening are the screening commencement age and number of screens (correlation coefficients were −0.865 and 0.714, respectively). Since the tissue radio-sensitivity reduces with age, the end age of screening does not result in noteworthy effect on total effective risk.
Conclusions: The regression model can be used to predict the total effective risk for clients within breast screening but it cannot be used for exact assessment of total effective risk. Graphical representation of risk could be an easy way to represent risk in a fashion which might be helpful to clients and clinicians.

1. Introduction

Radiation risk refers to the damage produced by ionising radiation due to energy deposition in tissues. The amount of damage is related to radiation dose, radiation source (e.g. whether it is internal or external), length of time of exposure, which organs are exposed to radiation and the individual's sensitivity which is influenced by age and gender [1]. Adverse health effects as a result of exposure to radiation can be classified into two groups: deterministic which follow high radiation doses and result in direct and predictable tissue damage; stochastic effects which follow low radiation doses and may result in cancer development [2].

There are two opposing risk models to estimate the risk from low radiation doses. The first adopts the linear no-threshold principle. According to this model any dose, no matter how small, can result in cancer. The second model proposes that there is a specific threshold for radiation-induced cancer, and below this threshold the radiation dose can be considered as safe [3]. It has been suggested that the best reasonable risk model to describe the relationship between the exposure to low energy radiation and solid cancers incidence is the linear no-threshold model (LNT) [2,4].

In 2010, the Health Protection Agency (HPA) reported that medical and dental X-ray procedures constituted 90% of man-made radiation sources to the United Kingdom (UK) population [5]. However, the medical radiation exposure to the United States (US) population increased by 600% from 1980 to 2012 [6]. Accordingly, there is a growing need for healthcare professionals to be more conscious of the risks associated with imaging when using ionising radiation for

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diagnostic purposes [7]. This is particularly true for mammography breast screening programmes where asymptomatic women are imaged [8]. Also, when screening frequency is increased, because of increased risk of breast cancer [9], radiation risk also increases as a direct consequence of mammography imaging. Extra diligence should therefore be exercised when assigning a woman into a high risk cancer category in which more frequent mammography screening is required. Overall, the radiation risk from screening mammography is considered to be low [10,11]. Nevertheless, the health profession needs to understand the radiation risks to the woman from mammography imaging, in order to justify serial imaging at any frequency level.

To date, radiation risk has tended to be expressed in terms of dose to the breast (mean glandular dose, MGD) which can be a difficult concept to understand by some imaging staff and referring clinicians. Equally the woman has to make an informed decision about participating in screening taking into account the potential harm the radiation might bring against the benefit of the programme [12].

The work presented here applies previously published data by M.Ali et al. [13] which measured the direct absorbed radiation dose from the examined breast, contralateral breast and 19 other organs across 16 FFDM machines to estimate lifetime effective risk of radiation induced cancer for the UK Breast Screening Programme. Here we develop the model further to establish a method for estimating & conveying lifetime induced cancer risk from breast cancer screening (from FFDM) for an average woman, with average breast size and density across a lifetime for a range of different FFDM screening scenarios. The method proposed is comprehendible and can be used by referring clinicians and breast screening organisations worldwide in the justification process and during the development of recommendations. Further, women will be able to make an informed decision on whether to attend breast screening.

2. Method

To calculate effective risk, organ dose data was required for all four mammography projections along with lifetime attributable risk (LAR) factors for all ages that screening takes place ranging from 25 years, the earliest probable age of screening for high risk clients in the US, to 75 years the latest age of screening end worldwide [13]. Two breast phantoms, attached to an adult dosimetry phantom, were exposed on 16 FFDM machines (Table 1) located in breast screening services within the UK. MGD was calculated; all other organ doses were measured directly using thermoluminescent dosimeters (TLD) as reported previously by M.Ali et al. [13]. LAR factors were calculated for a range of ages using a linear extrapolation method. Dose and LAR data were analysed to generate scenarios in order to calculate total effective lifetime risk values.

2.1. Phantoms

To replicate simulated breast thickness and shape in different positions, two breast phantoms constructed of polymethyl methacrylate-polyethylene (PMMA-PE) slabs were used. The Cranio-caudal (CC) phantom was semi-circular of 95 mm diameter and 53 mm thickness (32.5 mm PMMA and 20.5 mm PE); the medio-lateral oblique (MLO) was rectangular of $100 \times 150\ mm^2$ area and 58 mm thickness (32.5 mm PMMA and 25.5 mm PE). These breast phantoms simulate an average breast thickness with 29% breast density [14,15]. According to Yaffe et al. this density can be considered as the common breast density because they found that 95% of 2831 Canadian women have a breast density of less than 45% [16]. 280 calibrated TLD-100H dosimeters (Thermo Scientific, USA) were accommodated inside an adult ATOM dosimetry phantom (CIRS Inc, Norfolk, Virginia, USA) to measure the radiation dose received by 20 different body organs (indicated in Fig. 3). Harshaw TLD-100H dosimeters can measure radiation doses across a wide range (1 pGy–10 Gy) with linear response at this energy range (according to the manufacture guidelines [17]. The total uncertainty, due to sensitivity difference and consistency, associated with the detector readings is less than 5%. The ATOM phantom was positioned in contact with the breast phantom to simulate the female body (Fig. 1). MGD was calculated using the Institute of Physics and Engineering in Medicine (IPEM) method [18], which is based on the work published by Dance et al. [19].

Table 1
Study FFDM machines.

Machine Brand	Target/filter combination	Number of machines
Hologic Selenia	Mo/Mo	1
Hologic Selenia	Rh/Rh	2
Hologic Selenia Dimensions	W/Rh	2
GE Seno Essential	Rh/Rh	8
Giotto	W/Ag	1
Siemens Mammomat Inspiration	W/Rh	2
Total	16	

2.2. Exposing the phantom

The breast phantoms (and ATOM phantom) were exposed on 16 FFDM machines (see Table 1); exposures were repeated 3 times on each occasion and then averaged to minimise random error. Since the full automatic exposure control (including kV, mAs and target/filter combination) is recommend by the European commission [20], full automatic exposure control was used to expose the breast phantoms on each occasion.

2.3. Calculation of lifetime effective risk

Organ doses together with tissue specific LAR for the US population (BEIR VII phase 2 report) [4] were used to calculate effective risk from 25 to 75 years, using Brenner's equation [21].

$$R = \Sigma r_T H_T$$

Where R is the effective risk, r_T is the cancer LAR for tissue T per unit equivalent dose of that tissue, and H_T is the equivalent dose for tissue T. For each organ, the radiation dose was determined by averaging organ dose values from the sixteen FFDM machines. For breast tissue a total of both examined breast MGD and contralateral breast dose were used.

Since LAR factors are published for each decade of life and our method requires the tissue LAR value for each year it was necessary to estimate LAR values for the missing years. A linear relationship between LAR value for each decade of life was used (Fig. 2).

2.4. Data analysis

In order to get good statistical power, two hundred and seventy four different screening scenarios were proposed which comprised of different commencement/end ages (25–75 years) and screening frequencies. For each proposed lifetime interval, such as 25–75 years, 30–75 years, and 30–70 years, we scheduled three different screening categories with regard to screening frequency (annual, biennial, or triennial). Lifetime risk data, arising from the 274 scenarios were analysed in SPSS software (version 22.0, IBM, Armonk, New York, USA) to generate a mathematical regression model and relationship establishment between total effective risk and number of screens and commencement/end ages. The standard error of the estimate was calculated using SPSS software as the square root of the residual mean square to provide a measure of prediction accuracy of the regression model. Spearman's correlation was used to determine the effect of screening