

**REVIEW OF RADIATION RISK
IN BREAST SCREENING**

Report by a joint working party of the NHSBSP
National Coordinating Group for Physics Quality
Assurance and the National Radiological Protection Board

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1. SUMMARY

This review considers the risks and benefits of using ionising radiation to screen for breast cancer in the context of the UK National Health Service Breast Screening Programme (NHSBSP). Underlying radiation risk factors are derived from studies on North American women who received high doses of radiation for medical reasons. Age-specific lifetime risks of radiation-induced breast cancer are calculated for UK women. For women of screening age (50–70 years), this risk is approximately 1 in 100 000 per mGy. Radiation doses for women attending the NHSBSP are reviewed and taken to be on average 4.5 mGy per two-view screening examination. A risk and benefit calculation is undertaken. This takes into account the latest policy changes in the screening regime of the NHSBSP (ie the change to two views on every visit and to increase the upper limit for invitation from 64 to 70 years). The latest data from the NHSBSP are used to estimate the numbers of cancers detected by screening and the number of lives saved. The number of lives lost owing to radiation-induced cancers is also estimated. The ratio of lives saved to lost is calculated as a benefit–risk ratio of approximately 100:1. The reduction in this ratio for women who receive the highest expected radiation doses is also considered. It is concluded that the current and proposed screening regimes in the NHSBSP are justified in radiation protection terms.

2. INTRODUCTION

In the NHSBSP, mammography using ionising radiation is used to image the breast. The adverse consequences of ionising radiation are well established and there has always been a concern about their use in a screening programme whose aim is to detect cancer at an early stage. Any breast screening programme must be justified in radiation protection terms as well as in having a public health benefit.

At its simplest, justification in radiation protection terms means that the benefits of the screening programme exceed the risks associated with the use of ionising radiation.^{1,2} Justification applies for both a population and an individual basis. Before the NHSBSP was introduced, one of the issues that the Forrest report³ considered was the use of benefit–risk analysis concerning ionising radiation. Since then, a number of workers and groups have looked at the benefit–risk ratio, mainly in terms of the number of cancers detected and the number of cancers potentially induced by mammography. This is a relatively easy ratio to evaluate on both a population and an individual basis, but it does not give a complete indication of benefit or risk.

The NHSBSP, through its rigorous and comprehensive quality assurance programme, continues to evolve and improve. In recent years, the number of cancers detected has continued to rise, in part because of the introduction of a protocol under which two views are taken when women attend the screening programme on their first visit. In the meantime, patient doses have, on average, remained reasonably static. For women with large breasts, the recent introduction of modern, state of the art, mammographic units capable of adjusting the x-ray spectrum used to image the breast will reduce breast doses to this particular subgroup.

Since its inception, more data have been accumulated concerning the number of cancers detected by the screening programme. It is now possible, with varying degrees of accuracy, to deduce the impact of breast screening on reducing the mortality from breast cancer. The reduction of breast cancer mortality by 25% in the screened population is one of the targets of the *Health of the Nation*.⁴ A good indicator of benefit is the number of lives saved by the screening programme, which takes into account the reduction in mortality that results from detecting cancer at an early stage when the prognosis is much better.

One measure of the risk of breast screening is the potential number of fatal cancers induced by the use of ionising radiation in mammography. Because of the potentially harmful effects of radiation, the radiation dose received by women attending the breast screening programme has been regularly surveyed and is reasonably accurately known. However, the risk factor for the induction of breast cancer by ionising radiation is less accurately known and has to be deduced from the analyses of various epidemiological studies into groups of women exposed to radiation. These groups include the survivors of the atomic bombs dropped at Hiroshima and Nagasaki and various groups of North American women who received

high doses for medical reasons, eg from multiple chest fluoroscopies in the first half of the twentieth century. These data have been analysed to determine a risk factor applicable to the UK population.

The purpose of this document is to review the various sources of data required to evaluate the benefit–risk ratio for women attending the NHSBSP. Using these data, an estimate of the benefit–risk ratio for the screening programme on both a population and an individual basis will be made. The objective of the work is to verify that the breast screening programme is justified from a radiation protection perspective.

3. RATES OF CANCER INDUCTION

Radiation-induced breast cancers are indistinguishable from other breast cancers resulting from any other cause and are unlikely to appear until at least ten years after exposure. As a consequence, the potential for ionising radiation to induce breast cancer can only be estimated by observing whether groups of women who have been exposed to known levels of radiation suffer from an increased rate of breast cancer compared with those who have not been exposed. To have any chance of observing a statistically significant increase against the high natural incidence of breast cancer, such epidemiological studies have to be carried out on large groups of women who have received relatively high radiation doses and have been followed up for many decades. Groups that fulfil these criteria are the Japanese women who were exposed to radiation from an atomic bomb in the Second World War and the North American women who were given high doses of radiation for medical reasons (eg x-ray therapy for acute postpartum mastitis and multiple sessions of direct fluoroscopy for tuberculosis, mostly during the 1930s and 1940s).

Excess breast cancer rates have been seen in both these groups, the radiation appearing to have a multiplicative effect relative to the age-dependent natural baseline breast cancer rates. Japanese women, however, have a markedly lower natural incidence of breast cancer than women from western countries such as the UK and the USA, which makes it difficult to transfer radiation risks between these populations. So, in estimating the risks for women in the UK, the National Radiological Protection Board (NRPB) has chosen to use only the data from the studies of the North American women patients.⁵ These data suggest that an excess risk relative to the natural baseline breast cancer rate first appears ten years after exposure and then remains constant with time for at least the forty- to fifty-year period of follow-up. However, the constant excess relative risk was seen to be higher following exposure in childhood than exposures later in life, so two values were used: one for those exposed prior to the age of 20 years (1.03 per Gy for acute high dose exposures), which was about 2.5 times the value for those exposed at age 20 or older (0.42 per Gy). This simple two-step model used to describe the age-at-exposure dependence of the relative risk may appear a little crude but, at the time (1993), the NRPB considered that there were insufficient data available on which to base a more finely resolved age dependency model without a serious risk of introducing bias. More recent studies generally show relatively low values for the excess relative risk for women exposed after the age of 40 years that are in reasonable agreement with the value used by the NRPB for older women.⁶

Using the NRPB radiation risk model and the age-related baseline breast cancer rates and life expectancy statistics for women in the UK, it is possible to predict⁷ the age-specific lifetime risks of radiation-induced breast cancer for women, as shown in Table 1.

The risks can be seen to be very low for women currently invited onto the breast cancer screening programme (50–65 years old) at about 1 in 100 000 per mGy.

Table 1 Lifetime risk of radiation-induced breast cancer for UK women (screening ages are shown in bold)

Age at exposure (years)	Lifetime risk (per million per mGy)
5	43
10	43
15	43
20	18
25	18
30	18
35	17
40	16
45	15
50	14
55	12
60	10
65	8.0
70	6.1
75	4.2
80	2.5
85	1.2

There is evidence for most radiation-induced cancers that the effectiveness of the radiation in causing cancer is higher at the high doses (and dose rates) needed for epidemiological studies than at the lower doses usually experienced by the people for whom the radiation risk estimates are required. Since the North American women used in these epidemiological studies were exposed to total doses of up to a few gray in the course of their medical treatment, and since mammography doses are typically only a few milligray, the NRPB has applied a dose and dose rate effectiveness factor (DDREF) of 2. In other words, the risks derived from the epidemiological studies have been divided by 2 to obtain the risks appropriate for the mammography doses shown in Table 1.

There is some debate about whether it is appropriate to apply a DDREF of 2 in this particular situation. Firstly, analyses of the dose–response relationship in the studies of North American patients have shown that the data are consistent with a linear dose–response model (ie a constant dose effectiveness) over the ranges of dose observed.⁵ Secondly, although the total doses were high, they were mostly delivered as multiple small fractions spread out over many weeks or months, not as a single high dose delivered at a high dose rate. Some other bodies making recommendations on suitable radiation risks models (eg the US Environmental Protection Agency⁸) are known to advocate a DDREF of 1 for breast cancer. Use of a DDREF of 1 will double the risks for all ages at exposure shown in Table 1.

It should be appreciated that, although the risk estimates shown in Table 1 are judged by the NRPB to be the most appropriate for current application in the UK, there are other appreciable uncertainties in these values in addition to the choice of DDREF indicated above. In particular:

- the groups of exposed women in the epidemiological studies have not been followed over a full lifetime and there is little information on the time pattern of risks more than fifty years after exposure. This is important in estimating lifetime risks for those exposed in

childhood. However, it is less important for women exposed in later life (age 50 years or over) because the available epidemiological data allow lifetime risks to be calculated without the need for predicting future risks

- information on age-specific risks is sparse, leading to larger statistical uncertainties in these values than for risks averaged over a female population of all ages. Consequently, undue precision should not be attached to the values in Table 1, which have deliberately been quoted to only two significant figures
- it is unclear to what extent radiation risks may differ between women with a family history of breast cancer and other women. However, particularly for exposures at older ages for which radiation risks are lower, it is unlikely that genetic susceptibility would have a major impact on the average population risks used in this report
- there have been secular changes in the natural incidence of, and mortality from, breast cancer in recent decades. These may have affected the baseline rates for the UK population, relative to those used in this analysis.

Other national and international advisory bodies, for example the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR),⁹ the US committee on the Biological Effects of Ionising Radiations (BEIR V),¹⁰ the International Commission on Radiological Protection (ICRP)² and the US Environmental Protection Agency,⁸ have adopted different risk models, derived from the same or different epidemiological data (sometimes Japanese). When the UNSCEAR 1994⁹ and the BEIR V¹⁰ models are applied to the natural breast cancer rates and demographic data for women in the UK, the estimated lifetime risks of radiation-induced cancer for 50- to 65-year-old women are lower than the values shown in Table 1 by factors of about 2.5 and 6 respectively. However, there is known to be an error in the BEIR V model for breast cancer (it uses incorrect breast cancer incidence data from the Japanese atomic bomb survivor study⁵), and UNSCEAR has subsequently revised its risk model for breast cancer in its 2000 report.⁶ The effect of this revision is not stated explicitly in the new UNSCEAR report, but it seems likely to increase the risk predicted for 50- to 65-year-old women relative to that in the 1994 report.

For the purposes of the benefit–risk analysis in this report, it is proposed to use the following risk factors (interpolated from Table 1):

Age at exposure	Lifetime risk of cancer (induction per million per mGy of dose)
51	13.6
54	12.4
57	11.2
60	10.0
63	8.8
66	7.6
69	6.5

4. RADIATION DOSES IN THE NHSBSP

4.1 Dose to the standard breast

The methods used in the UK for the assessment of patient dose in mammography are described in the Institute of Physics and Engineering in Medicine (IPEM) Report No 59/2.¹¹ In the ‘standard breast method’, dose is calculated for a breast model which is 4.5 cm thick, with a central region comprising a 50:50 mixture by weight of adipose and glandular tissue and superficial regions of adipose tissue that are 0.5 cm thick. The mean glandular dose (MGD) for the standard breast is estimated from measurements with a 40 mm thickness of polymethylmethacrylate (PMMA), ie Perspex or Lucite. The MGD for the standard breast is useful for comparing doses between different mammography systems and for quality control purposes. It is one of the objectives of the NHSBSP that the MGD to the standard breast is 2 mGy or less.¹² The MGD to the standard breast is checked every six months on all systems used in the NHSBSP and the results of periodic national reviews are shown in Table 2.¹³⁻¹⁸

Table 2 Mean glandular doses to the standard breast for mammography systems in the NHSBSP from 1991 to 2001

Year	1991	1996	1997	1999	1999	2000/1	2000/1
Dose parameter	MGD at clinical settings (mGy)	MGD at clinical settings (mGy)	MGD at clinical settings (mGy)	MGD at clinical settings (mGy)	MGD at 28 kV Mo/Mo (mGy)	MGD at clinical settings (mGy)	MGD at 28 kV Mo/Mo (mGy)
Mean	1.28	1.36	1.38	1.40	1.36	1.56	1.46
Standard error	0.02	0.02	0.02	0.02	0.02	0.02	0.02
Median	1.20	1.31	1.38	1.37	1.35		
Standard deviation	0.35	0.34	0.32	0.28	0.28	0.38	0.29
Minimum	0.64	0.74	0.70	0.69	0.65	0.76	0.74
Maximum	2.60	2.46	2.40	2.60	2.60	3.40	2.50
No of systems	229	265	274	317	318	269	269
Proportion >2 mGy (%)	3.1	3.8	1.8	2.8	1.3	11.0	4.6

Although there have been many changes in equipment between 1991 and 2001, the MGD to the standard breast has varied only between 1.28 mGy and 1.46 mGy. In the earlier years, an x-ray spectrum produced by using a tube voltage of 28 kV and a molybdenum target with a molybdenum filter (28 kV Mo/Mo) was almost exclusively used both clinically and when measuring the MGD to the standard breast. However, since 1999 it has become much more common to use other x-ray spectra clinically. Currently, it is usual to measure the MGD to the standard breast at 28 kV Mo/Mo and at clinical settings. A fuller understanding of the implications of using alternative spectra is best appreciated by dose surveys on samples of screened women, as discussed in the next section.

4.2 Doses to individual women

Monitoring the MGD to the standard breast ensures that breast screening equipment is *capable* of achieving acceptable doses. The *actual* MGD received by the screened woman also depends on other factors, including

the breast size and composition, degree of compression, choice of kV, target and filter, and number of films taken. The method of assessing the doses to individual women is described in IPEM Report No 59/2.¹¹ The MGD per exposure (D) is calculated by using the postexposure mAs values to estimate incident air kerma (K) and using conversion factors (g -factors) calculated by Dance,¹⁹ as shown in equation 1.

$$D = Kg \quad (1)$$

The periodic measurement of doses for samples of women undergoing mammographic examinations is recommended in both screening and symptomatic mammography.^{20,21} Assessment of doses to samples of about 50 women attending for screening are measured routinely at most screening centres. A pilot study collected dose data for 4633 women from 92 screening units in 1994 and 1995.²² A later review reported on doses for 8745 women from 171 screening units in 1997 and 1998.²³ The average doses per film reported for these two reviews are summarised in Table 3.

Table 3 Average MGD per film from patient dose surveys across the NHSBSP (errors represent 95% confidence limits)

Projection	Mean MGD per film (mGy)	
	1994/5	1997/8
Oblique	1.98	2.03 ± 0.02
Craniocaudal	1.63	1.65 ± 0.02

4.3 Revised dose protocol

The conversion factors published in IPEM Report No 59/2¹¹ were obtained by computer simulation of a model breast with composition 50% adipose and 50% glandular tissues by weight (50% glandularity). Additional conversion factors that allow the extension of the protocols to breasts of varying glandularity and for a wider range of mammographic x-ray spectra have been published recently.²⁴ The data have also been extended to breasts of compressed thickness of up to 11 cm. To facilitate the calculation of MGD in patient surveys, typical breast glandularities are tabulated for women with different compressed breast thickness in the age ranges 40–49 and 50–64 years. Equation 2 is used to calculate the MGD per exposure:

$$D = Kgcs \quad (2)$$

The factor g is unchanged from that given in IPEM Report No 59/2 and corresponds to a glandularity of 50%. The c -factor corrects for any difference in breast composition from 50% glandularity. c -Factors have been calculated by Dance et al²⁴ for typical breast compositions at different compressed breast thicknesses in the age ranges 50–64 and 40–49 years. The factor s makes a correction for the use of an x-ray spectrum other than for a Mo/Mo target–filter combination. Software has been provided within the NHSBSP to facilitate the implementation of breast dose surveys using equation 2.²⁵ Dose surveys in the NHSBSP from 2001

onwards will be conducted using these new procedures. The benefit of the new protocol is that calculated doses will be more accurate. They will also show a systematic difference from those reported previously. For the largest breasts (thickest on compression), the use of the *c*-factor increases doses by approximately 30%. For the smallest breasts, the dose estimates are decreased by 11%. The overall effect is to increase the average doses by about 11% for craniocaudal views and by about 14% for mediolateral oblique views. The new protocol can be applied retrospectively, and the data shown for 1997/8 in Table 3 have been recalculated and are shown in Table 4.²⁶ Also shown in Table 4 is the average normalised dose ratio. The normalised dose ratio is the ratio of the MGD for the breast divided by the MGD for the standard breast on the mammography system used.

Table 4 Average MGD per film from patient dose surveys across the NHSBSP in 1997/8 recalculated after applying factors to correct for breast composition and spectra used (errors represent 95% confidence limits)²⁶

Projection	Mean MGD per film (mGy)	Mean normalised dose ratio
Oblique	2.36±0.03	1.73±0.02
Craniocaudal	1.86±0.02	1.40±0.02

4.4 MGD per examination

The MGD for a screening examination can be greater than the dose per film for a number of reasons. Firstly, extra films may be taken when a breast cannot be completely covered with a single film. Less commonly, an extra film could be a technical repeat taken at the time of screening. In the review of doses in the NHSBSP in 1997 and 1998, extra films were required for 4.5% of oblique views and 0.7% of craniocaudal views.²³ For the sake of simplicity, it is generally assumed that there is complete coverage of the breast for all exposures.^{22,23} This results in an estimate of the mean glandular dose which is proportional to the number of films taken.

The other reason for higher examination doses is that more than one view of the breast may be taken. Screening examinations in the NHSBSP are either one view or two view. A two-view examination is conducted at the first screen at the age of 50–52 years and comprises mediolateral oblique and craniocaudal films. Subsequent screens have usually involved a one-view examination comprising mediolateral oblique films. However, it has recently been decided that in future all screening will involve two views because of the resulting improvements in cancer detection. If more than one view of the same breast is taken, the mean glandular dose for each view is calculated separately and summed. The average screening examination doses have been calculated here and are shown in Table 5 using the data from the review of doses in 1997/8 and applying the new dose protocol.²³

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Table 5 Average MGD per screening examination in the NHSBSP in 1997/8 (composition and spectral correction factors were applied; errors represent 95% confidence limits)

Examination type	Number of women	Mean MGD per woman (mGy)	Mean age (years)
One view	5839	2.45±0.04	58.7±0.06
Two view	3087	4.13±0.09	53.3±0.09

For the purposes of the benefit–risk analysis in this report, it is proposed to use the following average doses for the screened population:

One view: 2.5 mGy per screening examination
Two view: 4.5 mGy per screening examination

4.5 ‘High dose’ subgroup

Screening must be justified not only in terms of the screened population as a whole but also for individual women. In practice, this means determining the dose for those women who are expected to receive the highest doses – the ‘high dose subgroup’. One identifiable subgroup of women who receive larger doses than average comprises those women with relatively thick breasts on compression. Reviewing the data collected for screening in 1997/8 shows that the small subgroup of women with compressed breasts greater than 95 mm thick receive doses of about 2.8 times the average for a given mammography system.

Another factor that affects the dose to these women is the dose to the standard breast for the equipment used, which ranged from 0.74 to 2.50 in the last national survey for systems in 2000/1. Although the quality assurance guidelines for the NHSBSP¹² require that the MGD to the standard breast should not exceed 2 mGy, a few systems were slightly above this limit. For the mammography system with the highest standard breast dose of 2.5 mGy, breast doses of about 1.7 times the average for all mammography systems can be expected. Thus, using this system one can expect that a few women with large breasts (100 mm thick) could receive doses of about 4.8 times the average for either a one-view or two-view screen (ie 2.8×1.7). If one assumes an average dose for two-view screening of 4.5 mGy, this high dose subgroup would receive 21.4 mGy. In an analysis of the data for the two-view screening of 3087 women, only one woman had a dose higher than this. This dose can therefore be regarded as an upper limit for what normally can be expected. By using modern equipment with automatic beam quality selection, such high doses should in the future be avoided for larger breasts.

For the purposes of the benefit–risk analysis in this report, it is proposed to use the following average doses for the high dose subgroup – assumed to be 0.1% of screened women:

One view: 12 mGy per screening examination
Two view: 22 mGy per screening examination

5. RISK AND BENEFIT OF SCREENING

5.1 Cancers detected/ induced

The numbers of cancers detected and induced by breast screening has been the subject of a series of publications by Law and Faulkner.²⁷⁻³⁰ Such a calculation is also made here using the induction rates shown in Table 1 and the doses discussed in section 3 along with the latest information on cancer detection rates. For the future, women in the NHSBSP will participate in seven screening rounds between the ages of 50 and 70 years. Table 6 shows the results of calculating the number of screen-detected and screen-induced cancers for each of seven rounds of screening. The following simplifying assumptions have been made:

- it has been assumed that a total of 2.0 million women are screened per year in seven screening rounds. This compares with the 1.49 million women actually screened in 1999/00.³¹ The numbers screened in each round are in proportion to the age distribution recorded for the female population in England and Wales in 1998.³² It is therefore implicitly assumed that the attendance rate is independent of age. At this time, relatively few women are screened over the age of 65 since a sixth and seventh round are not yet standard practice. Once screening is extended to these women, it is expected that there will be an increase in the number of women screened by approximately 33%, increasing the annual total to approximately 2 million
- a specific age has been chosen for each screening round. In practice, for each woman the first round could occur at any age, but is usually between 50 and 52 years, with subsequent rounds at three-yearly intervals
- the induction rates have been linearly interpolated for the specific ages assumed from the data given in Table 1
- the dose assumed for one-view screening is 2.5 mGy. The dose assumed for two-view screening is 4.5 mGy. However, at the time screening data were collected for the year 1999/00, two-view screening was standard practice in only the first round, and this is assumed in Table 6. Table 7 reflects the proposed practice of screening with two views in each round
- the doses assumed do not include a contribution due to mammography 'assessment' procedures. About 5% of women are recalled for assessment so that the total dose to the screened population could be considered higher by approximately that amount. However, it is thought to be better to consider assessment as a separate procedure with its own risk and benefit
- the detection rates were deduced from the *NHS Breast Screening Annual Review* for screening in the year 1999/00.³¹ The detection rates include both in situ and invasive cancers. The rate assumed for the first round is taken from the data reported for first screen detection in the age range 50–54 years where two-view screening was conducted. The data for subsequent screens have been linearly interpolated to specific ages, and in Table 6 are taken to be representative of one-view screening. The introduction of two-view screening is expected to increase detection rates.³³ The few

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programmes which have used two-view screening in all screening rounds have been reported to detect 25% more invasive cancers than one-view programmes.³³ However, there was only a 9% increase in the detection of invasive cancers in a comparison of one-view and two-view screening in a controlled experiment.³⁴ In Table 7, the detection rates for the second to seventh rounds have been increased by 25% to reflect the increase expected when two-view screening is fully introduced.

Table 6 Numbers of cancers induced and detected in seven rounds of screening (two views on first screen; one view on subsequent screens)

Screening round	1	2	3	4	5	6	7	All
Women screened	360 694	328 643	284 212	269 671	260 966	252 260	243 554	2 000 000
Average age (years)	51	54	57	60	63	66	69	59
Induction rate per million per mGy	13.6	12.4	11.2	10	8.8	7.6	6.5	
Dose (mGy)	4.5	2.5	2.5	2.5	2.5	2.5	2.5	
Induced cancers	22.1	10.2	8.0	6.7	5.7	4.8	4.0	61.5
Detection rate per 1000	6.4	4.4	5.4	6.3	7.3	8.3	9.2	6.6
Detected cancers	2308	1446	1535	1699	1905	2094	2241	13 228
Detected/induced	104	142	192	254	334	436	560	215

Table 7 Numbers of cancers induced and detected in seven rounds of screening (two views on all screens)

Screening round	1	2	3	4	5	6	7	All
Women screened	360 694	328 643	284 212	269 671	260 966	252 260	243 554	2 000 000
Average age (years)	51	54	57	60	63	66	69	59
Induction rate per million per mGy	13.6	12.4	11.2	10	8.8	7.6	6.5	
Dose for two views (mGy)	4.5	4.5	4.5	4.5	4.5	4.5	4.5	
Induced cancers	22.1	18.3	14.3	12.1	10.3	8.6	7.1	92.8
Detection rate per 1000	6.4	5.5	6.7	7.9	9.1	10.3	11.5	8.0
Detected cancers	2308	1808	1904	2130	2375	2598	2801	15 925
Detected/induced	104	99	133	176	231	302	394	172

The ratio of cancers detected to cancers induced is lowest for the younger women in the early rounds of screening because of the higher induction rates and lower detection rates. For the current screening regime, it is always above 100, and for the new regime it will fall below 100 only in the second screen.

5.1.1 High dose subgroup

The numbers of cancers detected and induced have been calculated for the high dose subgroup in Table 8. Even for this group, the ratio of cancers detected to induced is substantial. The number of women who receive a dose of this magnitude is currently very low, and is certainly less than 0.1% of those screened. It is expected that the introduction of mammography systems with automatic beam quality selection will greatly reduce the number of women receiving doses much higher than the average.

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Table 8 Numbers of cancers induced and detected for the high dose subgroup (two views on all screens)

Screening round	1	2	3	4	5	6	7	All
Women screened	361	329	284	270	261	252	244	2000
Average age (years)	51	54	57	60	63	66	69	59
Induction rate per million per mGy	13.6	12.4	11.2	10	8.8	7.6	6.5	
Dose (mGy)	22	22	22	22	22	22	22	
Induced cancers	0.1	0.1	0.1	0.1	0.1	0.0	0.0	0.45
Detection rate per 1000	6.4	5.5	6.7	7.9	9.1	10.3	11.5	8.0
Detected cancers	2.3	1.8	1.9	2.1	2.4	2.6	2.8	16
Detected/induced	21	20	27	35	47	62	80	35

5.2 Mortality rates

The numbers of cancers detected and induced by breast screening is not on its own a reliable indicator of the benefit–risk ratio. There are a number of reasons for this, but the main one is that not every cancer detected results in a life saved and not every induced cancer is fatal. Table 9 shows the results of a calculation of the number of lives saved by screening and the number lost as a result of radiation-induced cancers. The following simplifying assumptions were made:

- the target population is all women in the age range 50–70 years in the UK. One-third of the women are invited each year to one of seven screening rounds
- an acceptance rate (percentage of those invited attending screening) of 75% is assumed. This compares with the acceptance rate of 75.4% reported for 1999/00 by the NHSBSP³¹
- the numbers of cancers detected and induced are taken from Tables 6–8
- the mortality rate assumed in the absence of screening is 50%. (This is defined as the proportion of a group of women diagnosed with breast cancer who eventually die from breast cancer.) This compares with the ten-year relative survival rates for women with breast cancer diagnosed in the UK during 1981–5 of about 50%, as reported by the Office for National Statistics³²
- it is assumed that there is a breast cancer mortality reduction of 25% for women invited to participate in the screening programme. This is consistent with the *Health of the Nation*⁴ target of a 25% reduction in breast cancer mortality. Using a computer model of the NHSBSP, it has been predicted that the long-term (ie once a steady state has been reached) reduction in breast cancer mortality will be 24% in the age range 55–69.³⁵ (Note that this model did not take account of the introduction of two-view screening envisaged here)
- it is assumed that 75% of breast cancers arising in the screened population are detected by screening, with the remainder being interval cancers. While this is representative of the current screening regime, this figure can be expected to rise with the introduction of two-view screening and the age extension. A reduction in the proportion of interval cancers is likely to be associated with an increase in the mortality reduction in the screened population. Such factors contribute to the uncertainty in the mortality benefit explored in Table 10

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- it is assumed that the mortality rate for breast cancers arising in non-attendees and interval cancers is unaffected by screening and remains at 50%
- a consequence of the above assumptions is that a 25% breast cancer mortality reduction in the invited population is equivalent to a 33% reduction in the screened population, and a 44% reduction in women with screen-detected cancers. This means that the mortality rate for screen-detected cancers is reduced from 50% to 28%
- the screen-detected cancers include in situ cancers (21%). It has been implicitly assumed that there will be the same mortality reduction for these cancers as for invasive cancers. In practice, the mortality reduction for in situ cancers may be lower than for invasive cancers. However, it has been shown that 69% of screen-detected ductal carcinoma in situ (DCIS) is high grade, when the mortality reduction may be assumed to be the same as for invasive cancers.³⁶ Even if it is assumed that the other 31% of DCIS yields no mortality benefit, the reduction in the overall mortality benefit for all cancers would fall from 33% to only 31%. The possibility of a reduced mortality benefit for the detection of DCIS has therefore been considered as just one aspect of the uncertainty in the mortality benefit
- the mortality rate for radiation-induced cancers is taken to be that for screened women. However, because of the long delay in the appearance of these breast cancers, some may be beyond the twenty-year screening period. The effect of assuming that all the radiation-induced cancers are not detected by screening is explored in Table 10.

Table 9 Lives saved and lost by screening

	Two views in first screen only	Two views in all screens	Two views in all screens (high dose subgroup)
Age range (years)	50 to70	50 to70	50 to70
Screening rounds	7	7	7
Women in target population	8 000 000	8 000 000	8000
Women invited per year	2 666 667	2 666 667	2667
Acceptance rate	75%	75%	75%
Women screened per year	2 000 000	2 000 000	2000
Screen-detected cancers per year	13 228	15 925	16
Mortality rate in the absence of screening	50%	50%	50%
Mortality rate for screen-detected cancers	28%	28%	28%
Lives saved owing to screening per year	2910	3504	3.5
Induced cancers per year	61	93	0.45
Mortality rate for induced cancers	33%	33%	33%
Induced cancer deaths per year	20	31	0.15
Ratio of lives saved to lives lost	145	113	23

The mortality benefit–risk ratios are lower in Table 9 than the corresponding ratio of cancers detected to cancers induced in Tables 6–8. This is because only 1 in 4.5 screen-detected cancers results in a life saved, whereas 1 in 3.0 induced cancers leads to a death. The combination of these two effects is to reduce the ratios by a factor of approximately 1.5.

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The mortality reduction from breast screening on a population basis may be higher or lower than assumed above. In the Swedish two-county trial, a mortality reduction of 40% was reported for screened women.³⁷ More recently, a review of the impact of organised screening in seven Swedish counties reported a 40–45% reduction in breast carcinoma mortality among the women actually screened.³⁸ This corresponded to a 30% mortality reduction in the invited population. The impact of higher and lower assumptions about the mortality reduction is shown in Table 10 and Figure 1. This is shown as the ratio of lives saved to lives lost for two different assumptions concerning induced cancer mortality. In the first assumption, it is assumed that the induced cancers will be detected by screening at an older age, possibly over 70, and therefore have the same mortality rate as screened women. Such continued screening is encouraged by the NHSBSP, but invitations are not issued. In the alternative assumption, it is assumed that induced cancers mainly occur in older women beyond the age when invitations stop and are therefore not detected by screening. In this case, the higher mortality rate of 50% assumed for unscreened women has been applied.

Table 10 Effect of different mortality reductions on the ratio of lives saved to lives lost for two-view screening from 50 to 70 years

	Lower than expected mortality benefit	Expected mortality benefit	Higher than expected mortality benefit
Mortality reduction in invited women (%)	19	25	30
Mortality reduction in screened women (%)	25	33	40
Mortality reduction in screen-detected cancers (%)	33	44	53
Lives saved/lives lost (induced mortality as for screened women)	76	113	153
Lives saved/lives lost (induced mortality as for unscreened women)	57	75	92

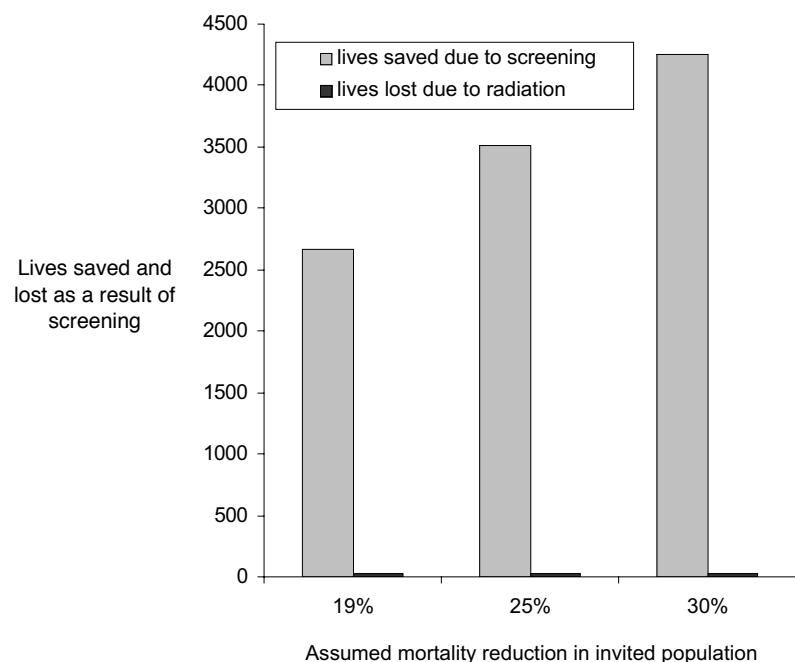


Figure 1 Annual number of lives saved and lives lost as a result of screening for different mortality reductions.

5.3 Years of life saved/lost

The above section considered the numbers of deaths from breast cancers to assess the benefit–risk ratio. However, an assessment of the number of years of life saved and lost provides an alternative and possibly better measure of benefit and risk. Using this measure, the benefit–risk ratios are likely to be much higher than ratios based on mortality. This is because of the long delay in the appearance of radiation-induced cancers – usually assumed to be at least ten years. A precise calculation of years of life lost and saved is beyond the scope of this review. However, Beckett³⁹ calculated these for the UK breast screening programme and found that the ratios based on years were approximately twice those based on lives. It would be reasonable to assume that the same would apply to the mortality ratios presented here. Jansen and Zoetelief^{40,41} have used a computer model to study the effect of screening on both the mortality reduction and the years of life gained. They found that annual screening from age 35 to 75 years resulted in both the mortality reduction and the years of life gained being reduced by 46%.

6. DISCUSSION AND CONCLUSIONS

This review has considered the radiation risk associated with breast screening. The rates of breast cancer induction have been recalculated and remain broadly similar to those previously published by the NRPB. However, there are large uncertainties in low dose cancer risk estimates. In its 2000 report,⁶ UNSCEAR stated that the uncertainty in risks for solid cancers overall following acute high exposures may be a factor of around 2 higher or lower, and that a further factor of 2 higher or lower may apply when estimating risks from chronic or low doses. On the other hand, dose aspects are well defined but have changed, particularly because of the proposal to introduce two-view screening in every round. As expected, this has almost doubled the radiation doses. However, the benefit assumed here has only been a 25% increase in cancer detection and, therefore, of mortality reduction. In practice, the benefit may be much higher if the additional cancers detected are small and therefore have an improved prognosis.

Screening with the new regime of two views every three years from age 50 to 70 years was found to be justified in radiation protection terms, with 113 lives saved for every life lost as a result of radiation-induced cancers. This ratio depends on the mortality reduction assumed. It falls to 76:1 if the reduction is 25% for screened women, and rises to 153:1 if the mortality reduction is 40%. As yet, it is too early to confirm the mortality reduction that will eventually be caused by breast screening in the UK.

The effect of changing the assumptions about whether induced cancers will have a reduced mortality as a result of screening is shown in Table 10. The true situation is likely to lie between the two extremes shown. If there is a great deal of screening activity beyond age 70, the benefit-risk ratios will be higher.

The following conclusions are reached for the new screening procedures in the UK:

- the risk of a radiation-induced cancer for a woman attending mammographic screening (two views) by the NHSBSP is about 1 in 20 000 per visit
- it is estimated that about 170 cancers are detected by the NHSBSP for every cancer induced
- the mortality benefit of screening exceeds the radiation-induced detriment by about 100:1
- for the very small proportion of women who receive the highest radiation doses, the benefit will exceed the risk by about 20:1.

In interpreting the above numerical conclusions, it should be borne in mind that they are based on an assumption about radiation risks that may be about a factor of 3 higher or lower than assumed. As a result, each numerical conclusion has a similar large uncertainty.

7. REFERENCES

1. *Recommendations of the International Commission on Radiological Protection*. Annals of the ICRP, Vol 1, No 3. International Commission on Radiological Protection. Oxford, Pergamon Press, 1977 (ICRP Publication 26).
2. *Recommendations of the International Commission on Radiological Protection*. Annals of the ICRP, Vol 21, No 1–3. International Commission on Radiological Protection. Oxford, Pergamon Press, 1990 (ICRP Publication 60).
3. Breast Cancer Screening. *Report to the Health Ministers of England, Wales and Northern Ireland by a Working Group Chaired by Sir Patrick Forrest*. London, HMSO, 1996.
4. *Health of the Nation: a Strategy for Health in England*. London, Department of Health, 1992 (HMSO).
5. National Radiological Protection Board (NRPB). *Estimates of Late Radiation Risks to the UK Population*. Document of the NRPB, Vol 4, No 4. Chilton, NRPB, 1993.
6. United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR). *Sources and Effects of Ionizing Radiation*. Vol II. *Effects. Annex I, Epidemiological Evaluation of Radiation-induced Cancer*. New York, United Nations, 2000.
7. European Commission. *ASQRAD – Assessment System for the Quantification of Radiation Detriment*. EUR 16644, CEPN-L-95/2. Luxembourg, EC, 1996.
8. US Environmental Protection Agency. *Estimating Radiogenic Cancer Risks*. EPA 402-R-93-076. Washington, DC, EPA, 1994.
9. United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR). *Sources and Effects of Ionizing Radiation. UNSCEAR 1994 Report to the General Assembly, Annex A. Epidemiological Studies of Radiation Carcinogenesis*. New York, United Nations, 1994.
10. Committee on the Biological Effects of Ionizing Radiations (BEIR V). *Health Effects of Exposure to Low Levels of Ionizing Radiation*. National Academy of Sciences, National Research Council. Washington, DC, National Academy Press, 1990.
11. Law J, Dance DR, Faulkner K, et al. *Commissioning and Routine Testing of Mammographic X-ray Systems*. York, Institute of Physics and Engineering in Medicine, 1994 (IPEM Report No 59/2).
12. *Guidelines on Quality Assurance Visits*. Sheffield, NHS Breast Screening Programme, 1998: 51–52 (NHSBSP Publication No 40).
13. Young KC, Ramsdale ML, Horton PW. *Review of Mammography Equipment and its Performance*. Sheffield, NHS Breast Screening Programme, 1992 (NHSBSP Publication No 24).
14. Young KC, Ramsdale ML, Rust A. *Mammographic Dose and Image Quality in the UK Breast Screening Programme*. Sheffield, NHS Breast Screening Programme, 1995 (NHSBSP Publication No 35).
15. Young KC, Ramsdale ML, Rust A. *National Survey of Mammographic Image Quality and Dose in the UK Breast Screening Programme*. Sheffield, NHS Breast Screening Programme, 1998 (NHSBSP Publication No 37).
16. Young KC, Ramsdale ML, Rust A. *Performance of Mammographic Equipment in the UK Breast Screening Programme in 1997*. Sheffield, NHS Breast Screening Programme, 1998 (NHSBSP Publication No 41).
17. Young KC, Ramsdale ML, Rust A. *Performance of Mammographic Equipment in the UK Breast Screening Programme in 1998/99*. Sheffield, NHS Breast Screening Programme, 2000 (NHSBSP Publication No 45).
18. *Performance of Mammographic Equipment in the UK Breast Screening Programme in 2000/1*. Sheffield, NHS Breast Screening Programme, 2003 (NHSBSP Publication in preparation).

19. Dance DR. Monte Carlo calculation of conversion factors for the estimation of mean glandular breast dose. *Physics in Medicine and Biology* 1990, 35: 1211–1219.
20. *Guidelines on Patient Dose to Promote the Optimisation of Protection for Diagnostic Medical Exposures*. NRPB Report Volume 10, No 1 (1999).
21. *Recommended Standards for the Routine Performance Testing of Diagnostic X-ray Imaging Systems*. York, Institute of Physics and Engineering in Medicine, 1997 (IPEM Report No 77).
22. Burch A, Goodman, DA. A pilot survey of radiation doses received in the United Kingdom Breast Screening Programme. *British Journal of Radiology* 1998, 71: 517–527.
23. Young KC, Burch A. Radiation doses received in the UK breast screening programme in 1997 and 1998. *British Journal of Radiology* 2000, 73: 278–287.
24. Dance DR, Skinner CL, Young KC, et al. Additional factors for the estimation of mean glandular breast dose using the UK mammography dosimetry protocol. *Physics in Medicine and Biology* 2000, 45: 3225–3240.
25. Young KC. *Breast Dose Surveys in the NHSBSP: Software and Instruction Manual*. Sheffield, NHS Breast Screening Programme, 2001 (NHSBSP Occasional Report No 01/10).
26. Young KC. Radiation doses in the United Kingdom trial of breast screening in women aged 40 to 48. *British Journal of Radiology* 2002, 75: 362–370.
27. Law J. Risk and benefit associated with radiation dose in breast screening programmes. *British Journal of Radiology* 1995, 68: 870–876.
28. Law J. Cancers detected and induced in mammographic screening: new screening schedules and younger women with family history. *British Journal of Radiology* 1997, 70: 62–69.
29. Law J, Faulkner K. Cancers detected and induced, and associated risk and benefit, in a screening programme. *British Journal of Radiology* 2001, 74: 1121–1127.
30. Law J, Faulkner K. Concerning the relationship between benefit and radiation risk, and cancers detected and induced, in a breast screening programme. *British Journal of Radiology* 2002, 75: 678–684.
31. *NHS Breast Screening Annual Review 2001: Informed Choice in Breast Screening*. Sheffield, NHS Breast Screening Programme, 2001.
32. Quinn M, Babb P, Brock A, et al. *Cancer Trends in England and Wales 1950–1999*. London, The Stationery Office, 2001.
33. Blanks RG, Moss SM, Wallis MG. A comparison of two view and one view mammography in the detection of small invasive cancers: results from the National Health Service Breast Screening Programme. *Journal of Medical Screening* 1996, 3: 200–203.
34. Blanks RG, Given-Wilson RM, Moss SM. Efficiency of cancer detection during routine repeat (incident) screening: two versus one view mammography. *Journal of Medical Screening* 1998, 5: 141–145.
35. Akker-van Marle E, Konig H, Boer R, Maas P. Reduction in breast cancer mortality due to the introduction of mass screening in the Netherlands: comparison with the United Kingdom. *Journal of Medical Screening* 1999, 6: 30–34.
36. Evans AJ, Pinder SE, Ellis IO, Wilson AR. Screen detected ductal carcinoma in situ (DCIS): over diagnosis or an obligate precursor of invasive disease. *Journal of Medical Screening* 2001, 8: 149–151.
37. Tabar L, Fagerberg G, Duffy SW, et al. Update of the Swedish two-county program of mammographic screening for breast cancer. *Radiology Clinics of North America* 1992, 30: 187–210.
38. Duffy SW, Tabar L, Chen HH, et al. The impact of organized mammography service screening on breast carcinoma mortality in seven Swedish counties. *Cancer* 2002, 95: 451–457.

39. Beckett J. Studies of benefit and risk resulting from the UK breast screening programme. PhD Thesis, University of Newcastle, 2000.
40. Jansen JThM, Zoetelief J. Optimisation of mammographic breast cancer screening using a computer simulation model. *European Journal of Radiology* 1997, 24: 137–144.
41. Jansen JThM, Zoetelief J. Assessment of lifetime gained as a result of mammographic breast cancer screening using a computer model. *British Journal of Radiology* 1997; 70: 619–628.