This paper aims to discuss the role of diagnostic imaging in screening protocols for early detection of cancer of the breast, colon and rectum, prostate and lung. The latest attitude of scientists and public health managers towards screening programmes is mainly driven by evidence results, but randomised trials are often difficult to start due to ethical reasons, and difficult to conclude because of the merging new technologies and the long time required. While mammography, even if sometimes controversial, is nowadays a consolidated tool for early diagnosis of breast cancer, other diagnostic techniques, such as low-dose computed tomography for detection of lung cancer, need to prove their efficacy and avoid extended times required to obtain evidence-based results.

Keywords: Mass screening (methods); diagnostic imaging; diagnosis; breast cancer; colon cancer; lung neoplasms; prostate cancer.

Introduction

The war that we are fighting against cancer has had poor results in decreasing related mortality, and the only success has been obtained by prevention campaigns aimed at smoking cessation policy, and early diagnosis obtained by screening programs. Primary prevention aims to reduce the incidence of cancer, but the only identified determinant of cancer risk is cigarette smoking and the international community has devoted a lot of effort to this field. Cancer mortality can be reduced either by diagnosing disease at an early and more ‘cureable’ stage or by increasing survival through improvements in therapy.

Screening for cancer involves the use of a test on asymptomatic individuals in order to classify them as likely or unlikely to develop the disease. Subjects with a positive test are submitted to further investigation to reach a final diagnosis, and those who are diagnosed positive for disease are treated. The goal of screening is to reduce mortality from the investigated disease among the screened population by means of early treatment of asymptomatic cases.

Before undertaking a screening trial for cancer, some important factors should be considered. The increasing demand for diagnostic work-up created by screening programmes has to be carefully evaluated: individuals with positive results need a prompt final diagnosis, since their anxiety will rapidly increase at any recall. The greatest workload of a screening program is generated from subjects with a positive screening test but with no cancer: the false-positive results. Their proportion in the screened population determines the specificity of the test.

The sensitivity of the diagnostic test has to be evaluated and compared with the gold standard that may refer to pilot studies or literature review. There may be several end-points of a screening trial, but only the reduction of cancer mortality in the screened group, compared to the control group, is free from the effects of bias: lead time bias, length time bias or selection bias. For this purpose, it is important that the management protocol of cancer in the screened and control groups be the same, in order to be able to separate the benefits of treatment and screening in the two groups. A treatment protocol for patients who entered...
Breast cancer

Breast cancer is a major public health issue worldwide: according to present estimates, one million women will be diagnosed with breast cancer this year. Clinical and pathologic considerations clearly demonstrate that survival following the diagnosis and treatment of breast cancer at an ‘early’ stage is much higher than when the disease is locally advanced or metastatic. A mammography can detect tumours at a clinically undetectable stage: such tumours have a very good prognosis and many can be cured by the correct treatment (Fig. 1).

In the late 1980s, the results from the early-randomised trials of mammographic screening were so promising that they led to the introduction of organised national screening programmes in many countries. Reports from seven trials involving more than 500,000 women confirmed a reduction of 20–30% in mortality from breast cancer in the group of women invited to join the screening (though not all were screened!). A few years ago, a couple of articles in Lancet\cite{2,3} raised doubts regarding the validity of the majority of these trials and led to a relevant public debate. These discussions had an enormous impact on public health practice, since many women participate in screening programs and any incorrect information given to avoid the screening program may cost lives.

The doubtful conclusions of Gøtzsche and Olsen were discussed by the Swedish AA\cite{4}, who reviewed their trials and confirmed a reduction in breast cancer mortality of 21%, persisting for a median time of 15.8 years. A working group of the International Agency for Cancer Research (IARC) concluded that many of the criticisms raised were unsubstantiated and that the evidence that screening by mammography reduces mortality from breast cancer in women aged 50–69 is undeniable. The reduction in mortality was estimated in 35% of women participating in screening programs. The United States Preventive Services Task Force (USPSTF) has also assessed the current evidence of mammographic screening, evaluating the quality of the available evidence and the performance of a meta-analysis. The reduction in breast cancer mortality among women invited to screenings was 23%. The USPSTF recommends a screening mammography every 1–2 years for women aged 40 and older, with or without clinical breast examination.

This indicates how conducting such large trials over many years can be difficult, particularly when technology, treatment and public health policy can change during their course. Nowadays, there is a general consensus that with the current evidence from randomised trials, taking account of limitations due to differences in compliance, the quality of mammograms, the methods of assessment and treatment, there is no reason to stop on-going or planned screening programmes.

Future efforts should be devoted to the evaluation of organised programmes of mammographic screening, to exploring methods that will ensure full participation and to the development of new technologies for early diagnosis. Many clinicians and analysts are concerned about the radiation dose given to the general population by extensive mammographic programs and are pushing to find alternative diagnostic techniques.

Mammographic screening is only one of the steps in the overall management of women with breast cancer: it is too often assumed that breast cancer mortality rates will decrease through more mammographic screening. But this goal can only be achieved with rigorous and high-

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**Figure 1** Screening mammography in asymptomatic patient: irregular, granular, polymorphic particles of microcalcifications with associated soft-tissue. Histology shows solid cellular proliferation with necrosis and calcifications in the thickened duct wall: foci of Ductal carcinoma *in situ*.

the trial should give the study the best standard clinical practice.
quality screening, diagnosis and treatment. Recognition of the importance of the multidisciplinary team in the assessment of mammographic abnormalities led to the development of integrated breast care centres, where dedicated radiologists, surgeons and pathologists can offer the best care to women with breast cancer and can quickly integrate technological and clinical up-dates for breast cancer diagnosis and treatment into their protocols.

**Colorectal cancer**

Colorectal cancer is the fourth most common form of cancer, occurring all over the world. There is a large difference in survival according to the stage of disease: 5-year survival in resected Dukes’ A is close to 80%, in Dukes’ B, if complete resection is feasible, it is 45% and in Dukes’ C it drops to 30%[5]. Colorectal cancer is an ideal target for screening, because the adenomatous polyp is a well-recognised pre-malignant lesion and its recognition and resection can prevent cancer development. Foecal occult blood testing (FOBT) and endoscopy have been tested as screening modalities. According to some randomised trials, there is evidence that FOBT is able to reduce colorectal cancer mortality by 16%, but the test has a high rate of false-positive results that reduce its clinical benefit. Sigmoidoscopy and colonoscopy have not yet clearly shown their efficacy in randomised trials, even if screening with sigmoidoscopy has been demonstrated to reduce the incidence of and mortality from colorectal cancer by 50% in case-controlled and non-randomised studies[6]. Costs, availability and patients’ compliance and discomfort are the major problems with the diffusion of colonoscopy as a screening test.

Computed tomography (CT) colonography, virtual endoscopy and the use of magnetic resonance imaging were recently proposed as diagnostic tools for screening. Many centres world-wide experimented with the radiologic approach and collected data on small series of subjects, comparing the results with endoscopic examination (Fig. 2). Anyway, also with these techniques, the patient has to undergo a full bowel preparation (the quality of the examination depends on the cleanliness of the patient’s colon) and colonic distension by air insufflation, these being the main causes of discomfort. The scan is performed in the supine and prone position during a single breath, and a significant dose of radiation is administered to patients, although low-dose protocols are under evaluation. Even if magnetic resonance avoids the radiation exposure required for CT scanning, magnetic resonance methods have been found to have significant disadvantages in terms of cost and complexity and have not yet achieved a diffusion as widespread as CT.

The sensitivity of CT colonography for polyps is dependent on polyp size (approximately 90% for polyps >10 mm, 80% for polyps 6–9 mm, and 50–55% for polyps ≤5 mm). The limited ability to detect small polyps, flat adenomas, or other mucosal lesions may reduce the efficacy in preventing cancer development and leads to repetition every few years. In addition, CT colonography has the potential to generate more procedures for follow-up of incidental extracolonic findings such as ovarian, renal, liver, and lung lesions, which have been reported in 15–41% of patients[7].

At present, there is no reason to propose CT colonography as a screening test, but future developments and technical improvements may lead to further studies. There is no agreement on screening for colorectal cancer and economic and industrial pressure, together with scientific squabbles, is making it difficult to convince the public health service and patients of the need for such a screening. We are missing the possibility of significantly reducing the number of 400 000 colorectal cancers that occur each year throughout the world.

**Prostate cancer**

After the introduction of prostate specific antigen (PSA) and the first reports on its efficacy, there is great pressure
for the screening of prostate cancer, although widespread implementation of screening programmes for prostate cancer cannot be recommended, according to available evidence. IUAC (International Union Against Cancer) has been in favour of this screening since 1991[8], but while screening by PSA is widespread in the USA, in the UK there is still a strong bias against it. This is mainly due to the lack of available results from randomised trials demonstrating an efficacy in the reduction of the mortality rate.

Ultrasound transrectal (TRUS) examination of the prostate can be combined with screening programmes in selected high-risk populations and is always essential in diagnostic work-up in subjects selected by means of a PSA screening test. Thus, the availability of the technique, together with a high quality therapy, is mandatory in guaranteeing the efficacy of screening. However, screening for prostate cancer at a population level would be expensive and consume a large proportion of available resources for health. The unpredictable outcome of prostatic cancer and the lack of demonstration that early detection and treatment could be effective are the reasons for the general caution in launching this screening.

**Lung cancer**

It has long been established that the best way to control lung cancer is to reduce cigarette smoking in the population. Although prevention and cessation strategies are obvious investments for intervention, there is presently no agreement on a control policy for subjects already at high risk due to either prolonged exposure to tobacco smoke or occupational exposure.

The difference in survival of lung cancer patients, when clinically diagnosed (10–16% at 5 years) or at early stages (>70% at stage I), led to speculation that high-risk individuals may benefit from early detection. In the 1970s, lung cancer screening programmes focused on chest radiography and several studies were established. But these trials had discouraging results, suggesting that screening by chest X-rays would not lead to a significant reduction in lung cancer mortality. Furthermore, both the Czech Trial[9] and the Mayo Lung Project[10], that compared chest X-ray to usual care, showed an increased number of lung cancers in the screened population, suggesting an overdiagnosis. Although no clear evidence of benefit from early detection emerged from these studies, they had a number of methodological shortcomings and they were considered ‘an imperfect basis for public policy’.[9]

The early reports on the efficacy of low-dose spiral CT gave new impetus and hope in the testing of screening for lung cancer[11,12]. In a Japanese study, 5-year survival of patients with lung cancer detected by CT screening was around 85%[12]. In the Early Lung Cancer Action Project (ELCAP), the 80% of Non Small Cell Lung Cancer (NSLC) diagnosed was in stage I and 96% of cancers were resectable, suggesting a possible similar survival of the screened patients[11]. However, in order to achieve such excellent results, thin-slice CT had to be performed in a high percentage of subjects with a complex algorithm of 3D reconstruction in order to assess minimal growth of detected nodules. In some cases diagnosis took up to 2 years and major expertise in fine-needle biopsy of small lesions was required.

Low-dose spiral CT seems to have a reasonable cost, acceptable levels of radiation exposure and high detection sensitivity: it has the potential to allow detection of sufficiently early stages to allow successful treatment of lung malignancies which would certainly be fatal otherwise. Efforts should be made to improve the diagnostic work-up on detected nodules, and to reduce costs, invasivity, time and radiation exposure needed to reach a final diagnosis (Fig. 3). The introduction of new diagnostic tools, such as positron emission tomography scan[13] and multidetector CT, might improve specificity.

![Spiral CT of the lung in asymptomatic smoker shows 7 mm solid nodule: T1N0 small cell lung cancer.](image)

**Figure 3**

There is an ongoing scientific diatribe on the need for randomised trials, but, as observed for breast cancer screening, they appear difficult to propose, for ethical reasons, and will need many years to give significant results on survival, while advancements in technology and new methods for screening of lung cancer will probably be proposed by the time the studies are concluded.

**Conclusions**

The great improvements in diagnostic imaging offer concrete opportunities to develop better screening techniques. Such advances in technology raise new issues, such as the problem of evaluating a method that will be outdated by the time the study is completed. The actual concept of evidence seems difficult to apply to screening...
for cancer, and alternative, reliable methods of evaluation need to be found if we intend to have a significant impact on public health.

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