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Significance of Radiologist´s Statement for the Interpretation of Plain Radiography in Cancer Patient Follow-up

A Randomized Study

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CONTENTS

Abbreviations

HRCT   =   high resolution computed tomography
CT   =   computed tomography
PET   =   positron emission tomography
MRI   =   magnetic resonance imaging
US   =   ultrasound
TAUH   =   Tampere University Hospital

1 Introduction

The constant growth in the number of new cancer cases and the improved treatment outcomes also serve to increase the number of patients in the follow-up phase. Earlier diagnosis of cancer and more effective treatments mean that the prognosis for many cancers has constantly improved. Greater proportions of patients are either achieving a complete recovery or surviving for a long time with their illness. After primary treatment cancer patients need years of sustained follow-up. The resources available are limited and will not be sufficient for follow-up at the degree of intensity at which it has so far been the case. A clearly increasing number of patients has required both development of treatment methods and a reappraisal of the service structure. It is necessary to evaluate what changes are required to present procedures in order that future cancer treatment and follow-up be maintained at least at its present quality.

From year to year there is an increasing number of patients in Finland, mostly aged, who are either currently suffering from cancer or who have at some time suffered from cancer. Even in the case of those who are deemed to have recovered, a relapse must always be suspected whatever the reason for seeking treatment for other illnesses may be. This may lead to radiological and other examinations to confirm or eliminate possible cancer. Thus cancer in the aged will consume more of the health care resources in addition to those required by the treatment of active cancer.

In follow-up the response to treatment and possible disadvantages of primary treatment are reviewed. The patient's overall recovery from cancer is also ascertained. The purpose of follow-up is to detect recurrences of cancer as early as possible, when treatment will still help, even though the disease has recurred. In the 1970s cancer treatment was mostly concentrated on hospitals. Follow-up was considered to be the province of the hospital first treating the cancer for the first five years. Cancers cause a heavy burden on hospitals (Hakala 1985). According to the prognoses of the Finnish Cancer Registry the number of new cancer cases was expected to increase at least until the year 2000. The need for resources has been exacerbated by the rapid development of medical technology and the increased use of specialities needed in the overall treatment of cancer. In the 1980s in Finland and also elsewhere in the world more attention was paid to cancer patient follow-up and the significance of its content. Research focussed on the investigation of follow-up in breast cancer patients. No effect could be demonstrated for inflexible follow-up programmed in advance on early detection of recurrence of cancer or on survival. Starting in the 1990s more attention was paid to other cancers such as lung cancer and colorectal cancer.

Radiological examinations have traditionally been part of the overall monitoring of cancer. It has been customary to radiograph patients as a routine procedure at each follow-up visit. However, there is no support in studies conducted so far, namely on breast cancer, for plain radiography monitoring rigidly programmed in advance. Indeed, routine examinations in cancer follow-up have been reduced and a more considered practice adopted. For example, in the follow-up of breast cancer chest radiography was recommended once a year for the first five years or if there was a suspicion of metastasis to the lungs (Lääkintöhallitus 1986). Nowadays in Finland we have at our disposal a national examination and treatment programme created by an expert group which determines procedure based on uniform and scientific research findings (Suomen Rintasyöpäryhmä ry 1999). A regional cancer diseases treatment system has been provided in Pirkanmaa Hospital District for diagnostics, treatment and follow-up in different cancers (Hakala 1998). According to the present recommendations routine examinations are not conducted, but diagnostic examinations are done as necessary.

The procedure for the interpretation of radiographies of lungs and skeleton varies among the different treatment units. In Finland there is no clear, common and harmonised practice. In addition to the interpretation of only a clinician or a radiologist it is possible that each of these views the plain radiographies separately, in which case the clinician later receives the radiologist's statement of images. The significance of the doctor interpreting plain radiography for cancer patients after primary treatment has not attracted scientific interest. It is not known if double interpretation benefits the patient, i.e. that his or her radiographs are viewed by a radiologist in addition to the clinician. On the other hand, there is no reliable information as to whether the interpretation of a clinician alone is sufficient (i.e. single interpretation). The significance of the radiologist and whether his or her interpretation is necessary has not previously been assessed.

The present study ascertains the significance to the patient and the organisation of the individual interpreting radiological examinations and especially plain radiography in following up cancer patients. The objective is to compare different practices in interpretation of plain radiography, primarily on medical, rather than economic grounds. The research is based on a randomised, prospective diagnostic experimental setting specifically conceived for this purpose. The findings are considered using the methods of clinical epidemiology.

2 Review of the literature

2.1 Occurrence of cancer

Cancer is a disease which is becoming more common in Finland and elsewhere in the world. The growth in the number of cancer patients was particularly marked in the first half of the 1990s, but prognoses would suggest that it will continue to grow until the year 2012. In 1970 the number of new cancer cases reported to the Finnish Cancer Registry was 11357, in 1990 it was 17375 and in 1995 it was 20110. In Pirkanmaa Hospital District the number of new cancer cases in 1970 reported 1073, in 1990 it was 1598 and in 1995 it was 1841 (Finnish Cancer Registry 1973, 1993, 2000). It has been estimated that the number of cancer cases in 2012 will be some 25000 in Finland (Engeland et al. 1993). Cancer may develop in any part of the body tissues and at any age. After the age of 40 the frequency of tumours increased steeply and cancer is typically a disease of the ageing body. The majority of cancer patients are over 60 years of age, only 1% of those with cancer are children (Pukkala et al. 1997). The overall incidence of cancer increases with age.

Since the 1960s there has been no change in the overall age adjusted incidence rates of cancer in men. By contrast there has been a slight increase in the overall incidence of cancer in women, but this has remained below that of men. Great changes have occurred in the incidence of different cancers. In men cancers of the stomach, oesophagus, lips and larynx have become less common. Nowadays the most common cancers in men are cancers of the prostate, lungs and bladder. These account for 48% of cancers in men, the proportion of prostate cancer alone being 28%. In women cancers of the stomach and oesophagus have become less common, as has cervical cancer since the 1960s. The most common cancers in women nowadays are cancers of the breast, the colon and the corpus uteri. These cancers account for 43% of cancers in women, and the proportion of breast cancer alone is 30%. It can be estimated that approximately every tenth Finnish woman will contract breast cancer during her life (Pukkala et al. 1997). It has been forecast that by the year 2012 the incidence of men's age-adjusted cancers will remain at its present level, while there will be a slight increase in the incidence of cancer in women (Engeland et al. 1993).

In Finland there are some 120000 living people who have or who have had cancer at some time in their lives, but who have recovered (Pukkala et al. 1997). The prevalence of cancer will grow continuously. This will be increased slightly by a rise in the population, but above all by the change in the age structure of the population and

also by the improvement in cancer treatment outcomes due to early diagnosis and continuous improvement in treatment. On the other hand the prognosis in general for cancer has improved due to early diagnosis and continuous improvement in treatment. A greater proportion of cancer patients can be completely cured of their cancers.

There will be a decrease in the numbers of those cancers, of the lung, the stomach and the oesophagus, for example, for which the prognosis is poor. Nevertheless cancer continues to be a serious and fatal disease. Some 10000 Finns die annually from cancer. Cancer is the basic cause of death of every fifth Finn (Tilastokeskus 1999).

2.2 Primary treatment of cancer

Different types of cancers require different treatments, and the same cancer may affect different individuals in a different way. The treatment of each cancer patient is planned individually. Factors determining the decision on treatment include the diagnostic data on the tumour, the size of the tumour, its histological characteristics and the degree of dissemination. The age of the patient and his or her other illnesses also influence the choice of treatment, as do the opportunities available for treatment and naturally the patient's own wishes in regard to the treatment planned.

In many cancers surgery is the first treatment. Radiotherapy is another important method for locally curative treatment of cancer. If necessary, the effectiveness of surgical treatment or radiotherapy can be enhanced by adjuvant treatments or if the cancer is not amenable to surgery or radiotherapy, adjuvant treatment is the treatment of choice. Adjuvant treatments include cytostatic or hormonal treatments. The biological treatment of cancer is also included in these. An effort is made to commence cancer treatment without delay. In some aggressive cancers a delay in the inception of treatment may render the planned treatment ineffective due to the growth of the tumour (O'Rourke and Edwards 2000). In addition to surgical treatment radiation treatment may be administered to many types of cancer to reduce the risk of local recurrence. If there is a delay in the commencement of radiation treatment after surgery there is an increased risk of local recurrence for breast cancer patients with lymph node metastases (Hartsell et al. 1995). Adjuvant treatments affect the entire system and are intended to inhibit metastases. Commencement of adjuvant treatment without delay has been shown to be important. In recent years adjuvant treatment has come to include drugs for increased efficacy compared to traditional treatments (Henderson et al. 1998, Douillard et al. 2000, Salz et al. 2000).

In health care cancer treatment is generally high priority owing to the seriousness of the disease. Treatments have generally been centralised in central hospitals and more

demanding treatments in university hospitals. Primary health care is in a crucial position as regards early detection and diagnosis, likewise in the implementation of follow-up and the organisation of palliative care. In the future the importance of primary health care will also increase in the active treatment of cancers and in their follow-up. All this constitutes challenges to cancer treatment, both qualitatively and organisationally, but it also means opportunities to achieve better treatment outcomes than before. In order to increase the efficiency of cancer treatment a special programme (STAKES 1993) has been drawn up for the various health care units. Co-operation between the various levels of health care and specialities is stressed in the treatment of cancer. In Pirkanmaa Hospital District regional co-operation programmes have been created since 1992. What continues to be essential in improving treatment outcomes is detection of cancer at as early a stage as possible, the accurate and immediate ascertaining of the dissemination of the disease and commencement of treatment as soon as possible.

2.3 Follow-up

The goals of follow-up are the earliest possible detection of a recurrence of the disease, and the identification of negative effects of the treatment. Moreover it is a goal of follow-up to provide the patient with many kinds of support so that he or she also recovers mentally and socially from his or her illness. It is an important goal of follow-up to promote the patient's recovery from his or her illness. Prearranged visits are the backbone of follow-up. The frequency of scheduled follow-up visits in different types of cancer varies. Extra visits are generally determined by patients' symptoms, their own observations or suspicion of recurrence of the disease as a result of diagnostic tests. The patient should be aware of which health care unit to turn to, if necessary. Follow-up serves to gather data on results needed for the monitoring of clinical quality and scientific research. In the evaluation of the achieving of follow-up goals the approach should be from the perspective of the patient. How does the patient benefit from follow-up? On the other hand it is possible to approach the issue from the effectiveness of the activity as a whole, because resources must be allocated to those actions from which there comes real benefit.

The degree to which the goals of follow-up are achieved depends largely on diseases and cases. In the literature there is an abundance of studies, mostly retrospective, on the follow-up of breast cancer and its significance for the detection of recurrence and survival after recurrence (Ciatto et al. 1985, Dewar and Kerr 1985, Marrazzo et al. 1986, Hietanen 1987, Tomin and Donegan 1987, Zwaveling et al. 1987, Rutgers et al. 1989, Snee 1994, Imoto and Jitsuiki 1998, Wheeler et al. 1999, Pivot et al.

2000). In addition to these considerations the effect of follow-up on the patient's quality of life has been estimated (Holli 1987, Kindler and Steinhoff 1989, GIVIO Investigators 1994, Grunfeld et al. 1996). For many other types of cancer there are evaluations of the applicability and significance of various methods of examination but the follow-up process as a whole has been little evaluated in terms of effectiveness and achievement of goals.

History and physical examination is an essential part of follow-up in all cancers. A careful examination of the treated area and of those parts of the body of significance to this and clarification of the patient's symptoms repeated each time lay the foundation in follow-up. According to the literature, history and physical examination have revealed as much as a good half of all recurring breast cancers (Horton 1984, Ojeda et al. 1987, Mansi et al. 1988, Schapira and Urban 1991, Schapira 1993, Joseph et al. 1998, Pivot et al. 2000). Physical examination of the patient in the detection of recurrences in breast cancer patients is part of follow-up. Physical examination and mammography repeated at regular intervals are mutually supportive methods of examination. Moreover, an effort is made to detect any tumour in the contralateral breast. In breast cancer follow-up the most important considerations are local status, symptoms indicative of metastasis and mammography. In follow-up the possible negative effects of primary treatment are identified in clinical examination. Pulmonary reactions are fairly common after radiation therapy for a malignant tumour. Combining radiation therapy with cytostatic treatment or anti-estrogen treatment has been found to increase pulmonary reaction (Marks et al. 1992, Bentzen et al. 1996, Trott 1999).

Follow-up radiological examinations represent an attempt to detect a recurrence of the disease as early as possible. Which plain radiography is selected on each occasion is largely determined by the patient's overall condition and the treatability of the disease. Despite new radiological methods plain radiography continues to be primary in examining the lungs and the skeleton. In the follow-up of breast cancer patients, for example, routine chest radiography has been abandoned. The significance of plain radiography has been dubious as far as early detection of a recurrence is concerned. On the other hand it has also not been possible to show that plain radiographies would have improved the treatment outcome directed at the disease (Holli 1987). More laboratory and isotope tests than before are done as required by physical examination and the patient's symptoms.

The frequency and duration of follow-up vary between patients and cancers. In several cancers routine follow-up has been shown not to have any effect on recurrence as earlier detection of recurrence or length of survival. In breast cancer patients routine follow-up detected some 22% of recurrences after treatment (Brøyn and Frøyen 1982, Pivot et al. 2000). Holli and Hakama (1989) noted that 2.9% of regular visits ultimately

resulted in a confirmed diagnosis of first recurrence whereas the prevalence was significantly higher (14.7%) for spontaneous visits. Loong et al. (1998) noted that 79% of breast cancer patients suffering a recurrence had symptoms at the time the recurrence was found. In routine follow-up no difference was observed in the length of disease-free time between breast cancer patients with or without symptoms, suffering a recurrence (Rutgers et al. 1989, Pivot et al. 2000).

Westeel et al. (2000) noted that intensive follow-up slightly improved non-small cell radically operated asymptomatic lung cancer patients' survival compared to that of patients with symptoms in 3-year follow-up. In follow-up after small cell lung cancer 59% of all recurrences of the disease were detected in extra visits. The researchers stressed the importance of history and physical examination in the discovery of recurrences of the disease (Perez et al. 1997). Accurate and carefully arranged follow-up appeared ineffective in the detection of relapse in preclinical large cell lymphoma patients (Weeks et al. 1991).

2.4 Plain radiography and recurrence of cancer

Recurrence of cancer may occur at the site of a locally treated tumour or as metastasis elsewhere in the body. The tendency to metastasis is an essential biological characteristic of the tumour depending on time and the size of the tumour. Among the more common varieties of primary tumours which metastatise readily to the lung are carcinomas of the stomach, breast, lung, prostate, colon, liver, thyroid, pancreas and kidney (Spencer 1985), but virtually any malignant tumour may reach the lung (Hammar 1988). Pulmonary metastasis seldom causes the patient any symptoms, especially in the early stages. Thus symptoms do not indicate early pulmonary metastases. Usually pulmonary metastases present as one or several spherical nodules whose size may vary. According to the literature it has been noted in post mortem examinations that pulmonary metastases tend to locate themselves on the periphery of the lungs (Scholten and Kreel 1977, Crow et al. 1981). In most cases there is more than one metastasis and they are frequently in the lower parts of the lungs (Libschitz and North 1982). The incidence of macroscopically diagnosed endobronchial metastasis is low, but if microscopically diagnosed metastases are also made into account the incidence rises considerably (Braman and Whitcomb 1975). In endobronchial metastasis the patient may present with a cough, hemoptysis or secondary pneumonia.

Lymphangitis carcinomatosa means the dissemination of a cancer through the pulmonary circulation to the lymph nodes and lymphatics. Tumour cells are also frequently encountered in the binding tissue structures inside the pulmonary tissue.

Various cancers may cause lymphangitis carcinomatosa, but in most cases it is connected to adenocarcinoma. The most common causes are cancer of the breast, lung, stomach and pancreas (Libshitz and North 1982, Spencer 1985).

The most common causes of pleural metastases are lung cancer, breast cancer and lymphoma and cancers of the ovary and stomach (Matthay et al. 1990). Pleurametastasis has been diagnosed in 82% of lung cancers with pleural effusion. The presence of pleural effusion in a patient with lung cancer is not always a sign of inoperability (Cantó et al. 1985). Of breast cancers among all the cases with pleurametastasis the majority had the metastasis on the same side as the breast cancer (Cantó-Armengod 1990). Metastasis of the pleura may present as local nodules or malignant effusion (Raju and Kardinal 1981). Pleural metastasis frequently causes patients to suffer pain associated with breathing.

The skeleton is one of the most common areas to be affected by metastasis of cancer. Pains in the bones and sensitivity to knocking are symptoms highly indicative of metastasis in the skeleton. However, skeletal metastasis has been shown to be symptomless in its early stages in 64% of the breast cancer patient (Stierer and Rosen 1989). Tomin and Donegan (1987) showed that just over one third of skeletal metastases were symptomless. Skeletal metastases are the most common with breast cancer, but there is considerable variation of incidence numbers. The disease generally disseminates via the blood, and direct dissemination from the breast tumour to the rib cage, for example, is less common. The most typical sites for skeletal metastases of breast cancer are the ribs, the spine and the hip. Fractures are often the most significant complication in skeletal metastases. It is especially important to diagnose fractures of the spine and of long bones in time as they may result in invalidity for the patient and indirectly cause death.

If the patient's symptoms and sputum do not provide reliable evidence of lung metastasis and if bronchoscopy is not an advisable procedure because of its invasive nature, plain radiography is the most important means of examination for lung metastases in the follow-up phase of cancer. Detection of nodules in the chest radiographies depends on the location of the change. If the nodule is over 6 mm in diameter and is located in the plain radiograph in the intercostal space it can almost always be discerned, but if the change is on the rib it is more difficult to see (Gray et al. 1978). According to Simeone et al. (1977) lung metastasis was not detected in plain radiography of more than a half of patients with extensive malignant melanoma. Lung metastases could be detected within one month of the plain radiography in the post mortem examination.

There are several studies in the literature in which a recurrence of breast cancer was detected in less than 2% of all routine follow-up chest radiographies (Chaudary et

al. 1983, Hietanen 1986, Rutgers et al. 1989, Vestergaard et al. 1989, Løgager et al. 1990, Moskovic et al. 1992). Generally lung metastasis as the first sign of a recurrence is symptomless (Winchester et al. 1979, Chaudary et al. 1983, Ciatto and Herd-Smith 1983, Ciatto et al. 1985, Hietanen 1986, Andreoli et al. 1987, Tomin and Donegan 1987, Virkkunen et al. 1987, Kamby et al. 1988, Vestergaard et al. 1989, Løgager et al. 1990, Moskovic et al. 1992, Pivot et al. 2000). Pleural malignant effusion is generally found in patients with symptoms (Ciatto and Herd-Smith 1983, Hietanen 1986, Virkkunen et al. 1987). In pulmonary metastases of breast cancer which were the first sign of recurrence of the disease, no difference was found in the size or distribution of the metastases between patients with and without symptoms (Virkkunen et al. 1987). The ability of plain radiography to reveal lymphangitis carcinomatosa has been shown to be modest because the radiological findings are extremely unspecific. Plain radiographies have shown a normal result for half of the patients although the histopathology showed lymphangitis carcinomatosa (Goldsmith et al. 1967).

A recurrence of breast cancer is seldom found by plain radiography (Hietanen 1986, Ojeda et al. 1987). Plain radiography and other diagnostic examinations should be done for those breast cancer patients who have experienced new symptoms during follow-up, or for whom there are other clinical findings (Zwaveling et al. 1987, Kindler and Steinhoff 1989, Rutgers et al. 1989). Chest radiographies at frequent intervals are of importance at the stage when breast cancer has disseminated, when the benefit derived from treatment can be estimated in part from the plain radiography. The significance of routine chest radiographies in the follow-up of patients with cancer of the thyroid has also been questioned in the detection of recurrences of the disease (Powell et al. 1994, Lorenzen et al. 1998). According to Perez et al. (1997) recurrences of small cell lung cancer were detected mostly by history and physical examination, and by plain radiography in only 12%. In the follow-up of patients with Hodgkin's disease chest radiographies served to detect 23% of recurrences and the majority of recurrences by history or physical examination (Torrey et al. 1997). Most recurrences of cancer in melanoma patients are found by history and physical examination. According to the researchers the significance of chest radiographies is limited (Weiss et al. 1995).

It has been shown that a single posteroanterior radiograph is sufficient in the assessment of pulmonary metastases of melanoma. A lateral chest radiograph was not shown to contribute anything further to the diagnosis (Collins et al. 1993). A similar result was obtained in the case of chest radiography follow-up of patients suffering from thoracic lymphoma (Dobson et al. 1997).

Unexpected findings have been obtained through chest radiography in one quarter of hospital patients and the information obtained from the plain radiography affected the treatment of rather more than half of the patients. In this study material 22% of the

patients were suffering from cancer (Berlowitz et al. 1989). Geitung et al. (1999) reported unexpected findings in 20% of the chest radiographies in their own data, but 45% of these was of no clinical value. Daily routine chest radiographies of patients in intensive care were found to alter treatment plans in 37% of examinations (Marik and Janower 1997). The WHO has estimated that approximately half of all plain radiography made throughout the world is chest radiography (WHO 1983). In extensive material of chest radiographies a radiological finding was ascertained in only 7% without the patient having any chest symptoms. The majority of these images had been made as routine examinations and only one third of patients had symptoms or other findings outside the are a of the chest cavity (Geijer and Göthlin 1998).

Radiographies of the skeleton are insensitive in indicating metastases, especially if these are small (Citrin 1980). Most skeletal metastases develop in the medullary part and changes only develop on the cortex of the bone at a relatively late stage. Plain radiography is therefore insensitive in revealing early skeletal metastases. The change in the trabecular bone must exceed 1.5 cm in diameter and the mineral content of the bone must be locally depleted by at least one half before the change is visible in a plain radiography. In the cortex, smaller metastases are discernible in a radiograph (Edelstyn et al. 1967). If the destruction of the bone cortex is seen to exceed 30% in a radiograph, this indicates a high fracture risk.

2.5 Comparison of various radiological and other methods of examination

Postpneumonectomy recurrence either on the site of the surgery or in the mediastinum is frequently difficult to discover with a plain radiograph, in which the excised side may be opaque and possible new changes of the disease cannot be discerned because of the weak contrast differentiation of the radiograph. After removal of a lung it was found that plain radiography indicated a recurrence of lung cancer in 42% of cases, computed tomography (CT) revealed all recurrences either prospectively or retrospectively (Glazer et al. 1984). CT easily showed residive lung cancer postpneumonectory attrition in the region of the bronchial stump or elsewhere on the side of the operation. For 67% of patients the exact size and location of the recurrence influenced the planning of radiation therapy (Glazer et al.1984). CT also proved to be more reliable than plain radiography in the follow-up of resected lung cancers (Görich et al. 1990). There is typically a situation after radiation treatment of lung cancer in which it would be desirable to be able to estimate the size of the tumour and the response to treatment. The situation is complicated by the presence of reactive changes of the radiation sensitive

lung, when it is difficult to distinguish between a possible tumour and a reaction to radiation. The radiation changes in the lung can be discerned sooner and more widely in CT than in plain radiography (Schnabel et al. 1978, Pagani and Libschitz 1982, Libschitz and Shuman 1984, Bell et al. 1988, Frija et al. 1988, Ikezoe et al.1988, Slanina et al 1988, Schmitt et al. 1992). In the follow-up with radiography of lung cancers treated by radiation unjustified suspicion of recurrence of cancer occurred in 29% of cases. CT distinguished between radiation reaction and recurrence of cancer in almost all cases (Bourgouin et al. 1987). The appropriateness of CT has been presented in the literature as preferable to plain radiography for the follow-up of lung cancer patients after radiation treatment (Bourgouin et al. 1987, Lyn et al. 1992, Schmitt et al. 1992, Langendijk et al. 1998), but the weakness of the method in comparison to pathological findings after neoadjuvant concurrent chemoradiotherapy has been shown by Lee et al. (2000). Positron emission tomography (PET) proved to be more accurate than CT or plain radiography in the follow-up of lung cancer patients after radiation (Hebert et al. 1996).

From plain radiographies it has been possible to measure the size of lung cancers treated with radiation and so to estimate the response to treatment in less than half of cases. Likewise it has been possible to take tumour measurements using CT in many more cases. It is difficult to estimate the size of centrally located tumours from radiographies. Likewise atelectasis of the surrounding lung beside the tumour complicates the estimation of the tumour itself (Lyn et al. 1992, Langedijk et al. 1998). Measurements from chest radiographies are appropriate for measuring very peripheral lung tumours, especially if there is no atelectasis of the lung tissue on the tumour (Langendijk et al 1998). The measurability of treated small cell lung cancers has been shown to be almost 20% lower with chest radiographies compared to CT images (Dajczman et al. 1994). Researchers recommend that the size of almost all tumours in patients suffering from small cell lung cancer should be measured both pre and post treatment using CT. For the assessment of treatment response in lung cancers after chemotherapy CT is generally preferable to plain radiography (Pujol et al. 1992). In the 1980s promising results were already achieved with magnetic resonance imaging (MRI) in distinguishing between atelectasis of the lung and actual tumours (Tobler et al.1987, Shioya et al. 1988). So far there is not sufficient proof whether MRI is appropriate for the measuring of the tumour and assessment of treatment response after radiation treatment. Preliminary findings on the applicability of PET in the assessment of response after radiation treatment of lung cancers have been presented. It has been shown that this complements the information gained through plain radiography and CT, especially in tumours which are difficult to discern with other methods of examination (Hebert et al. 1996).

When radiographing lymphoma patients after treatment it is common to observe extra change in the treated area. To decide whether this is a malignant change, an insignificant relic or scar is a common practical problem. To achieve certainty it is necessary to take samples or control radiological examinations. CT has proved more reliable than plain radiography for lung imaging in the assessment of mantle field radiotherapy or cytostatic treatment situation for patients with Hodgkin's disease both in showing residive and in distinguishing it from radiation changes (Heron et al. 1988, Thomas et al. 1988), and in the assessment of treatment response in general after treatment for lymphoma (Khan et al. 1989). Examining the mediastinum with ultrasound (US) has actually proved more reliable than CT when assessing the treatment response of lymphoma (Wernecke et al. 1991). With US it has been possible to distinguish suspicious lymph nodes of less than 1 cm which appeared to be normal with CT. The study by Wernecke et al. (1991) clearly demonstrated the superiority of US compared to plain radiography. The inactive MRI pattern appears to be more reliable, although microscopic foci of residual disease may be missed (Rahmoni et al. 1993). The pulmonary hilar lymph nodes and their size can be ascertained more reliably than with conventional CT with a one mm thin section made from the hilar areas. By examining the surrounding structures using morphological criteria it is possible to distinguish the lymph nodes more clearly and to measure their size and on that basis estimate possible metastasis (Shimoyama et al. 1997).

In the ascertaining of lung metastasis plain radiography has shown the dissemination of the disease to an accuracy of 86%, but more lesions have been found with conventional tomography of the entire lung (Didolkar et al. 1977). Lung metastases vary in size, most changes being less than 2 cm across, but of all metastases more than half are 5 mm or less (Crow et al. 1981). Because of its high image resolution CT is clearly more sensitive as a method for diagnosing lung metastases than plain radiography. CT shows up small nodules in the lung which later turn out to be benign more than plain radiography and the specificity for the examination remains low (Chalmers and Best 1991).

CT has proven to be more reliable than plain radiography, especially in detecting small peripheral metastases or those situated close to the pleura (Muhm et al. 1978, Schaner et al. 1978). Conventional linear tomography of the entire lung area showed up fewer lung nodules compared to CT (Muhm et al. 1978, Chang et al. 1979). MRI has been shown to be as sensitive as CT in showing lung metastases (Feuerstein et al. 1992). CT of the lungs also finds other than metastasis nodules, for example scars and other benign infiltrates, than does plain radiography. Even though the radiographies were normal, lung nodules were found in 13% of CT images of which 20% were estimated to be malignant in preoperative examination (Chalmers and Best 1991). With

spiral CT technique it is now possible to detect more metastases than with conventional CT technique because it examines the entire lung at one arrest of breathing. More nodules of 5 mm across have been found with spiral technique than with conventional CT technique (Remy-Jardin et al. 1993). If accelerated examination of the images at the workstation (cine viewing examination) is combined with spiral technique it significantly increases the capacity to distinguish pulmonary nodules that are smaller than or equal to 5 mm in diameter (Tillich et al. 1997), while segmentation or extraction of vascular structures subsequently facilitates detection of lung nodules (Croisille et al. 1995). On the other hand, the more accurate the technology used, the more benign nodules are also found. These non-metastatic additional findings frequently result in further examinations. Using high resolution computed tomography (HRCT) and microangiographic technique makes it possible to show the feed vessel leading to the metastasis and so to confirm a suspicion of metastasis (Milne and Zerhouni 1987, Meziane et al. 1988). By combining the result of plain radiography with that of the spiral or HRCT it has been possible to improve sensitivity in the distinguishing between benign and malignant nodules, but it has not been possible to improve specificity (Seeman et al. 1999). It is possible to find endobronchial metastasis through CT on a virtual endoscope, but not with other radiological methods. PET has yielded promising results in distinguishing between malignant and benign lung changes in patients who are known to have or who are suspected of having melanoma metastasis (Damian et al. 1996). PET has been shown to be more sensitive in the assessment of lung lesions when compared to CT and MRI, but PET is not specific in relation to the malignant nature of the change (Kim et al. 1999).

If metastases of the pleura appear as small nodules they may go totally unobserved in plain radiography, but are generally discerned in CT and MRI. Effusion of the pleura can be seen with all radiological methods.

There is no ideal method of examination in detecting skeletal metastasis. If skeletal metastasis is suspected, the most sensitive method is skeletal scintigraphy. It is an advantage of the method that in addition to sensitivity the entire skeleton can be included in one image. In skeletal scintigraphy more than one third of all results were false positives. These were caused by benign bone changes. Individual positive scintigram results should be confirmed by plain radiography (Citrin 1980, Galasko 1995). Radiographies and scintigrams are mutually complementary examinations in both diagnosis of metastases and in assessing treatment response. If the scintigram yields a positive result which could not be confirmed by plain radiography it is advisable to use CT or MRI as further methods (Galasko 1995).

MRI has been shown to be better than scintigraphy in revealing skeletal metastases in the region of the spine (Avrahami et al. 1989, Algra et al. 1991, Gosfield

et al. 1993). Tamada et al. (2000) found that MRI of the entire body revealed skeletal metastases more often than scintigraphy with the exception of the region of the ribs. Since the finding of scintigraphy does not always correlate with the activity of the real disease, it has been necessary to develop new, more efficient methods. Bone metabolic markers such as gla protein (BGP) and procollagen I carboxyterminal peptide (PICP) serve to contribute to the search for metastases (Koizumi et al. 1995). In the follow-up of breast cancer a rise in CA 15.3 marker level has been generally shown to indicate active state of the disease, especially as metastases (Wheeler et al. 1997).

It is common in images after treatment for lymphoma, both Hodgkin's disease type or not, to find residual mass, the incidence of which according to the literature is 15% to 64% (Radford et al. 1988, Trédaniel et al. 1988, Glenn and Kumar 1991). CT was incapable of showing whether residual mass was mere fibrosis or whether the remaining mass was active lymphoma in over one half of patients in remission (Israel et al. 1988). It has been shown that rapid responses in the treatment of lymphoma seen through radiography and other methods are an important prognostic factor (Armitage et al. 1986). Gallium imaging has been perceived as among the most significant non-invasive techniques in detecting residual activity after treatment for lymphoma (Kaplan et al. 1990). Subsequent research findings do not support the superiority of gallium imaging compared to other methods (Hagemeister et al. 1990, Hill et al. 1993). MRI appeared to distinguish reliably between fibrosis and active disease, especially in Hodgkin's disease and to provide clinically useful prognostic information (Hill et al. 1993). But signal intensity patterns in MRI reflect gross histologic characteristics after treatment of lymphoma and cannot be considered specific (Rahmoni et al. 1993). Single photon emission computed tomography (SPECT) gallium scanning has been shown to distinguish active disease more reliably than CT and to predict the progress of the disease better than does CT, especially in metabolically active lymphoma (Vose et al. 1996).

In plain radiography an exceptional breadth of the mediastinum in Hodgkin's patients who have received radiation treatment persisting one year after radiation treatment or chemotherapy combined with radiation treatment did not appear to predict a recurrence of the disease. On the other hand, if patients had received only chemotherapy the exceptional mediastinum width seen in chest radiography was statistically significant in predicting a recurrence of the disease (Radford et al. 1988).

A single metastasis of the lung can be treated surgically by resection if further dissemination of the disease has not been found, and this serves to prolong the patient's survival (Gromet et al. 1979, Harpole et al. 1992). The researchers cast doubts on chest radiographies in revealing metastases because one third of metastases was found only in retrospective examination (Gromet et al. 1979). A thoracoscopic examination of cancer

patients whose lung metastases had been found by CT produced further information in almost one half of cases so that the treatment planned on the basis of radiological examinations was changed in 40% of cases (Rau et al. 1998). Metastases of malignant melanoma in the lung can be found before metastases appearing elsewhere in the body produce clinical signs. For this reason it has been considered that there is a place for plain radiography as a follow-up evaluation method in malignant melanoma (Webb and Gamsu 1977), but before commencing to treat malignant melanoma metastases with immunotherapy or surgery it has been recommended to conduct CT in order to detect other possible metastases (Heaston et al. 1983).

2.6 Diagnostic methods and effect of findings on patients' survival and death

In a study of colorectal cancer patients ascertaining whether chest radiography, liver CT and colonoscopy contribute anything in five-year follow-up, it was found that the radiological imaging and colonoscopy examinations did not show any advantage. Equally good results were obtained from carcinoembrionic antigen (CEA) and faecal occult blood testing (Schoemaker et al. 1998). The research findings presented earlier likewise do not support intensive follow-up (Mäkelä et al. 1995, Ohlsson et al. 1995, Kjeldsen et al. 1997). Although more pleural and skeletal metastases were detected in breast cancer patients in intensive follow-up than in only clinical follow-up, no difference was found between the two arms regarding five-year mortality figures (Rosselli Del Turco et al. 1994). The GIVIO Investigators (1994) found 31% of metastases in intensive follow-up of breast cancer patients in symptom-free phase and 21% in symptom-free patients in only clinical follow-up. However, no difference was found between the arms regarding survival.

According to randomised studies follow-up of the symptom-free breast cancer patient which is based on frequent or abundant imaging or laboratory tests does not improve the prognosis compared to less frequent and less routine imaging follow-up (GIVIO investigators 1994, Rosselli Del Turco et al. 1994). A similar result was obtained for follow-up of melanoma patients in retrospective examination (Weiss et al. 1995).

Although routine chest radiographies have shown lung metastases of symptom-free breast cancer, no proof of improved prognosis has been obtained (Hietanen 1986, Ciatto et al. 1989, Rutgers et al. 1989). Finding symptom-free metastases in the follow-up of breast cancer patients has not been shown to have any effect on the patients' survival (Ciatto and Herd-Smith 1983, Hietanen 1986, Andreoli et al. 1987, Løgager et

al. 1990). There would not appear to be any effect on the patient's survival from whether the response of the lung cancer patient to radiation treatment was measured using plain radiography or CT (Langendijk et al. 1998).

When a comparison was made between breast cancer patients with and without symptoms, no significant difference in survival was found between those whose recurrence of the disease had been found first in the lung or the pleura (Virkkunen et al. 1987, Løgager et al. 1990). The size of the primary tumour and the nodal status in the first five years after diagnosis are of equal significance to the prognosis for breast cancer and the survival of the patient. The original size of the tumor is of prognostic significance only for five to ten years, but not more (Nab et al. 1995). It has been shown that in average survival time there is no significant difference between those patients in whose lung changes appropriate for intrathoracic lymph node metastases in addition to lung metastases compared to those patients in whom only mediastimun or metastases of hilar areas had been detected (Webb and Gamsu 1977). For detection of recurring breast cancer only by mammography the five-year survival rate is 95% and by only palpation 74% (Stacey-Clear et al. 1992).

Localization of skeletal metastases below the lumbosacral junction predicts subsequent metastases of the visceral organs (Yamashita et al. 1991) and shorter survival (Yamashita et al. 1995). Searching for symptom-free skeletal metastases has been shown to be pointless in breast cancer patients, since although the treatment is begun at the symptom phase, no difference in survival has been shown compared to starting before symptoms have appeared (Tomin and Donegan 1987, Stierer and Rosen 1989). A clear correlation was established in the period between detection of breast cancer and skeletal metastasis observed in scintigraphy of the skeletal remission time and the patients' survival (Janicek and Shaffer 1995).

Factors influencing survival prediction include screening for cancer, improved treatability of tumours, advances in treatment methods and increase in the number of aged cancer patients rather than frequent follow-up and the associated radiological and other methods of examination. The studies of radiological imaging and other methods of examination are mostly retrospective and nonrandomized and the results depend more how to select the patients and on other biases than the imaging and other procedures during follow-up.

2.7 Factors affecting the reading accuracy of plain radiography and discerning of changes

Radiologists' reading accuracy was investigated by a re-evaluation of both chest and bone radiographies. The accuracy for chest radiographies was 80%, and there was no difference observed between radiographies of patients with and without symptoms. For bone radiographies the accuracy was 90% for patients with symptoms (Tereso-Tess et al. 1981). Several metastases with symptoms appeared to improve diagnostic accuracy, while individual metastases without symptoms appeared to go unnoticed. No influence on accuracy was established from localisation of lesions or morphological characteristics (Tereso-Tess et al. 1981). Diagnostic accuracy with radiography proved clearly better for intrathoracic adenopathy and multiple lung metastases in follow-up of breast cancer patients with symptoms than with patients having no symptoms. Diagnostic accuracy was also found to be better with bone radiographies if patients had symptoms (Valagussa et al. 1982).

Impivaara et al. (1998) researched detection of small shadows on the lung and changes in the pleura and differences in classification from chest radiographies between radiologists. These researchers report 69% unanimity on all lung opacities. Difference between readers was not statistically significant. Readers were in agreement regarding changes as frequently as the same reader on different occasions. Tudor and Finlay (1999) investigated improving accuracy in reading chest radiographies by the same radiologists at intervals of 24 hours. The accuracy increased on the second occasion but this did not reach statistical significance. On the other hand, if the clinical data on the patient were available to the radiologist, this was seen to improve accuracy and increase unanimity on interpretation even though no statistical significance was reached in the findings (Tudor et al. 1997). Robinson et al. (1999) studied differences in radiologists' interpretations of first aid chest radiographies. They established considerable differences in interpretations between evaluators. Greater unanimity was found between radiologists for bone radiographies than for chest radiographies. According to experimental assessment by Young and Marrie (1994), radiologists' interobserver variability did not improve with increasing experience in interpretation of pneumonia radiographies. In the assessment of pneumoconiosis changes strictly according to the International Labour Organisation (ILO) classification significant differences were found between evaluators (Attfield et al. 1986, Bourbeau and Ernst 1988, Ducatman et al. 1988, Parker et al. 1989, Ducatman 1991, Jacobsen 1991). The difference was due to the complexity of the classification and the effect of aspects of image quality in general on the detection and classification of minor changes. In the interpretation of chest

radiographies it has been established that clinical history information from the patient increased the number of true positives found from 38% to 84%, but that the number of false positives also increased (Doubilet and Herman 1981). Experimental examinations have been used to establish which factors cause false negatives in the visual scanning detection of nodules in the lung. According to the researchers, 30% were due to the examination technique of the image field. A slightly smaller proportion (25%) was due to failure to identify change and the largest error (45%) was connected to decision-making on the change (Kundel et al. 1978). The image processing used in the examination of chest radiograph did not appear to have the effect of increasing diagnostic performance (Krupinski et al. 1998). Berbaum et al. (1989) investigated the accuracy of orthopaedists and radiologists in interpreting plain radiographies. They found that if information was available on the localisation of the patient's symptoms at the time of analysing radiographies, this served to improve accuracy for both radiologists and orthopaedists, but especially for orthopaedists assessing possible fractures from bone radiographies.

Changes may go unnoticed in radiographies due to features of anatomy, poor image quality, paucity of history information, lack of radiographies for comparison and the reader's subjective characteristics. Double reading can improve accuracy in detecting shadows on the lung from chest radiographies, but the method has not been seen to be cost-effective, and it nevertheless does not eliminate the effect of subjective factors (Hessel et al. 1978).

In general little is known of the effectiveness of follow-up of cancer patients, and the findings are contradictory and generally negative. Research so far has covered the biological disease well, but has not addressed the patient's physical, mental and social well-being. The research findings so far on radiological actions in cancer patient follow-up have focussed on individual examination methods or have compared the ability of different methods with one another in their ability to detect changes in the disease. There are no research findings on the overall efficacy of radiology in cancer follow-up, nor on the overall burden occasioned by this activity.

3 Purpose of the study

The treatment and follow-up of cancer patients impose ever increasing quantitative and qualitative burdens on radiological imaging and diagnostics. The predicted increase in the number of cancer patients and the development of treatment methods from the present situation demand an evaluation of the structure of radiological services. Focussing radiological measures more accurately and appropriately than at present on the needs of cancer follow-up must be based on reliable research data on the content and effectiveness of actions.

The procedures for interpreting plain radiography varies in Finnish hospitals. At the Department of Oncology of Tampere University Hospital (TAUH) cancer patients' plain radiographies are first examined by a clinician and then a radiologist, each separately. There is research data available on the importance of radiographies in cancer patient follow-up, but not on the importance of the individual interpreting them. The present study proposes to ascertain the significance of double reading both for the patient and for the organisation.

For the purposes of the research an experimental research setting was created in which patients were randomised into two arms when they were transferred from primary treatment of cancer to follow-up. The interpretation of a clinician and a radiologist (double reading) was compared to that of a clinician alone (single reading). The aim of the research was to estimate the effect of the statements made by the radiologist on the follow-up phase of the cancer patient

1.   on the use of material and human resources
2.   on the findings in plain radiography, the time of their detection and the consequences
3.   on the treatment given to the patient for the recurrence of the disease and the point at which this is commenced
4.   the patient's physical well-being
5.   the patient's survival

4 Materials and methods

4.1 Area, population and organisation of cancer treatment in Pirkanmaa Hospital District

The research data consist of those cancer patients who in the period 1991–1997 transferred after primary treatment from the Department of Oncology of Tampere University Hospital to follow-up and who came within the Pirkanmaa Hospital District. The average population during the period 1991–1997 was 436000, i.e. 8.6% of the population of Finland. Women account for 225000, which is 51.7% of the total population of the hospital district (Tilastokeskus 1998). New cases of cancer for the period 1991–1997 in the whole of Finland were 141102, of which 52.4% were women. In the Pirkanmaa Hospital District there were 12592 new cases of cancer, of which 52.7% were women (Finnish Cancer Registry 1993, 1994, 1996, 1997, 2000).

Pirkanmaa Hospital District comprises 35 member municipalities. Regional hospitals are situated in the towns of Mänttä, Valkeakoski and Vammala. There are also two health centre hospitals under a specialist, Hatanpää Hospital in the city of Tampere and Nokia Hospital. There are 19 health care centres in the area. There is also a system of private doctors which is partly an alternative to the public health care system.

Cancer follow-up in Pirkanmaa Hospital District is divided among various health units. Follow-up is arranged in the health centres, regional hospitals and the University Hospital. The location at which follow-up is conducted is determined primarily by the patient's domicile, but also by the cancer, and the primary treatment given. There is also follow-up in the practices of private doctors. General recommendations exist regarding follow-up location, but these have not been completely implemented.

Although the primary treatment had been administered to the patients elsewhere than at the Department of Oncology of TAUH, these patients were included in the study if their follow-up was undermade there.

4.2 Randomisation

For the purposes of the present study an experimental research setting was created in which the cancer patients were randomised into two arms for the period 1.11.1991–31.5.1995, when they transferred from primary treatment for cancer to follow-up at the Department of Oncology of TAUH. The basis for randomisation was the day in the patients' personal identity codes. Lots were drawn in advance as a result of which those

born on odd-numbered days were assigned to the arm with double reading and those born on even-numbered days were assigned to the arm with single reading. The plain radiographies of patients in the double-reading arm were first reviewed by a clinician and then by a radiologist, each separately. The radiographies of patients in the single-reading arm were examined by a clinician only, who might, if necessary request a statement from a radiologist. The date for randomisation was set at the day on which primary treatment ended or the day of the first visit to follow-up, always assuming that plain radiographies had not been made of the patient between the end of primary treatment and the first follow-up visit. When a patient transferred to follow-up a research sticker was attached to the radiograph referral at the date in question. After plain radiography the personnel returned the radiographies of patients to the outpatient clinic and also the radiograph referral of the single-reading arm with a note that a statement could be obtained if necessary. The patients continued to participate in the research after randomisation until follow-up ended either in death, moving away, change to a different follow-up level or other similar reason, or then until 31.12.1997.

4.3 Patients

The research included those patients who had transferred to follow-up at the Department of Oncology of TAUH with no limitations on age or sex. Requirements were that patients should have a microscopically confirmed cancer with no restrictions regarding type or stage of disease. The only cancer to be excluded from the study was cancer of the testes as the follow-up of this type of cancer is different from that of other cancers. It was required that the cancer had received primary treatment, either curatively or palliatively.

The total number of randomised patients was 1115. The annual statistics of TAUH showed that 1366 patients transferred to follow-up at the Department of Oncology from primary treatment, thus a total of 251 patients were not included in randomisation. A further 246 patients were excluded from randomisation due to erroneous randomisation. For these the most common reason for erroneous randomisation was wrong time. Patients were either randomised before the end of primary treatment or after the first follow-up visit. Thus a total of 122 patients (66/56) were excluded from the study. There were 82 (43/39) patients transferring to follow-up after residual treatment. They were not originally part of the study and they were eliminated from the study. There were 15 (9/6) patients without microscopic confirmation of cancer, and they were not included in the study. There were 14 (6/8) patients erroneously randomised, while transferring to follow-up elsewhere. Two

patients in the double reading arm died before the first follow-up visit. Ten statements on plain radiographies were issued erroneously without request and these patients were removed from the data. One patient with cancer of the testes was randomised into the double reading arm, and by reason of the type of his cancer he was not part of the research.

Altogether of those patients removed for reasons of randomisation errors 132 should have been included in the research, 66 in each arm. In the final data there were 869 patients, i.e. 86.8% of the actual number for randomisation.

4.4 Clinical and radiological follow-up

The outpatient clinician ascertained the state of the patient's disease on the basis of history information and his or her own physical examination and on other examination information available. Radiological follow-up comprised plain radiography and special examinations either agreed on at the previous visit or undermade in view of the patient's changed condition at the time. Plain radiographies were made at the Department of Radiology and sent to the Department of Oncology, where they were always interpreted first by a clinician. The radiographies belonging to the double-reading arm were interpreted afterwards by a radiologist. The radiographies for the single-reading arm were interpreted by a radiologist only on clinician's request. Special radiological examinations were also conducted at the Department of Radiology with the exception of mammography, magnetic imaging and angiography. The patients' other test, for example, laboratory and isotope examinations were determined on the basis of the respective situations according to the clinician's assessment regardless of the research arm to which the patient had been assigned.

4.5 Data collection

The research was randomised and prospective. Data were collected retrospectively from the medical histories. Data on cause of death were made additionally for 33 patients from the register of cause of death of Statistics Finland. Data collection ceased on 31.12.1997. The duration of follow-up for the patients included in the study varied. The author undertook all data collection for the study on a data collection questionnaire formulated for the purpose. The researcher looked at the plain radiographies only after medical histories had been collected, thereby avoiding the influence of reinterpretation on original information. Before the actual data collection was begun, the questionnaires

were tested on the information of 50 patients and the availability of information in medical histories was checked. The questionnaires consisted of sections for basic information and follow-up information.

The core section of the questionnaire elicited information on cancer diagnosis, the degree to which the disease had disseminated and primary treatment. The follow-up section of the questionnaire was completed separately for each year of follow-up on the total events of the year. Information on the first visit of each year was entered, likewise the date of the radiological examination and the date of the last follow-up visit of the year. All visits within the year were noted for type of visit, number of doctors at the outpatient unit, number of radiological examinations made for various reasons and number of separately requested radiologists' statements on plain radiography. Special examinations occasioned by uncertain findings in plain radiography were noted separately. For the first detection of suspicion of cancer, information noted included date, nature of visit, person making the finding, the patient's symptoms, size and location of the finding and date of confirmation. Data were also collected on the treatment of recurrent phase of cancer, its follow-up especially with regard to radiological examinations, and separately requested statements from radiologists and data on death. The total number of core information questionnaires was 869, and the total number of follow-up questionnaires was 3145.

The author accomplished the data collection over an uninterrupted period on a full-time basis. The author tested the reliability of data recording by completing new questionnaires for 200 patients attending the first examination and comparing them with information contained in the originally completed questionnaires.

4.6 Protocol applied

Primary treatment of cancer generally refers to the treatment given during the first four months after diagnosis. Primary treatment is surgery and radiotherapy or medication or various combinations of these. Response to primary treatment is considered complete if all cancer changes have disappeared and the response so achieved has lasted at least four weeks. Partial response refers to a reduction of at least 50% of disease changes and no progression of the disease has been found and the length of response is at least four weeks. The response to primary treatment compared to the initial situation is considered to be unchanged if disease changes are reduced by less than 50% or if the increase of changes noted in the progress of the disease has been less than 25% and no new areas with changes have been found. The disease is deemed to be progressive if after primary treatment an increase of more than 25% in changes has occurred (Miller et al. 1981).

Follow-up refers in the present study to the follow-up arranged at the Department of Oncology of TAUH. Follow-up conducted elsewhere is noted only in cases of a recurrence of cancer. The first day after termination of primary treatment was made to be the first day of follow-up, and this day was used in calculating the follow-up years. Follow-up visits refers to visits to a doctor at the cancer outpatient unit. The first follow-up visit was made to be the first visit after primary treatment either at a prearranged time or an extra spontaneous visit. A visit was considered to be a routine follow-up visit if it took place in keeping with the recommended follow-up schedule for each type of cancer. An extra follow-up visit was made to be one deviating from the planned routine follow-up. A follow-up visit counted as extra if, because of a finding on a routine visit, the doctor requested the patient to attend again. An extra visit might be occasioned by the patient him- or herself, either by coming direct to the clinic or by coming on another doctor's referral. For each year of follow-up the date of the last follow-up visit was entered. Once follow-up had ceased at the Department of Oncology of TAUH, no further follow-up of the patient elsewhere was noted. The survival of the patients remaining in the study was noted according to the situation on 31.12.1997.

For each year of follow-up the date of the first radiological examination was noted, this frequently being the same as that of the first follow-up visit.

The radiological examinations were analysed separately for plain radiographies and special examinations. The examinations were counted together for each year of follow-up for subject of radiograph and name of examination. Plain radiograph refers to an image of the lungs, abdomen or skeleton made by a radiographer. After plain radiography a radiologist issues a statement on the examination. Special examinations refers to fluoroscopy, ultrasound, computed tomography or magnetic resonance imaging performed by a radiologist and the taking of samples in connection with these. Mammography is also a special examination although in practice it is performed by a radiographer. After special examinations the images are generally reviewed by the radiologist conducting the examination. Routine tests refers generally to plain radiographies and special examinations arranged in advance and forming part of the recommended schedule for each respective cancer. Extra examinations are necessitated by suspicion of recurrence of cancer or problems caused by primary treatment. Radiological examinations requested by someone else than the doctors of the Department of Oncology were noted for each year of follow-up either as examinations connected to cancers or conducted for other reasons. If for any reason the patient was admitted to the ward of the Department of Oncology during follow-up the radiological examinations conducted on behalf of the ward were noted as were examinations requested by the outpatient unit.

For findings indicating a recurrence of cancer both findings considered certain and suspected findings were noted. In recurrence of cancer a distinction was made between local recurrences and metastases. Separate note was also made of new cancers or suspicion of these. Information on the finding included recording the date of observation, the type of visit, the individual making the observation, the patient's symptoms and the means of observation. Separate mention was made of observation of the finding in plain radiography or special examination. The size, number of changes and localisation of the finding were also noted. The finding was considered a certain recurrence of cancer, if it was confirmed radiologically with a repeat plain radiograph, by special examinations, histologically or other method, or if it was decided on the basis of the finding to begin treatment. The follow-up treatment for recurrence of cancer was entered in the same way as primary treatment. In the present study recording of the actual follow-up data was discontinued on the date on which a recurrence of cancer during follow-up after primary treatment was confirmed. For the present study data on recurrence of cancer were collected from plain radiographies, but also from special examinations. If the recurrence or suspicion of recurrence of cancer was found clinically, through laboratory tests or by some other method, these events were recorded in the same way as radiological findings. Findings indicative of something else than recurrence of cancer were noted for radiological examinations. For all findings the consequence was noted, i.e. whether it was decided to commence treatment or whether the situation was to be monitored. In the present study laboratory tests and isotope tests are not differentiated in detail.

The overall performance status of the patient was assessed at follow-up visits using the Zubrod scale (Zubrod et al. 1960). Almost without exception information was available from medical histories. On the Zubrod scale 0-1 indicates that the patient can cope with all normal tasks and is entirely able to move, to work and that activity is restricted only in demanding physical tasks. Grade 2 indicates performance status in which the patient is mobile and capable of taking care of him- or herself, but unfit for work. Grade 3 indicates that the patient is no longer entirely capable of taking care of him- or herself. Grade 4 indicates that the patient is entirely immobile. In the present study the patient's general performance status was recorded only on the last follow-up visit of each follow-up year on the basis of assessment, and no possible variation in performance status during the year was recorded.

4.7 Methods

In the examination of the five follow-up years information on all follow-up visits was added together, for example, types of visit, changes in outpatient doctors, and numbers of radiological examinations. Moreover the number of follow-up events per patient year (follow-up year) was counted. The number of patient years counted together for each randomised arm is the length of follow-up. Patient years are reduced by deaths and other removals from the follow-up. Patients dying in the first follow-up year were made to have been in follow-up for only one third of a year due to the high risk of death a short time after primary treatment. Patients who died or left follow-up in other follow-up years were made to have been in follow-up for half of that year. Thus, for example, the number of patient years accruing in the fourth year of follow-up is the number of patients at the beginning of the fifth year of follow-up with the addition of half times the number of those leaving follow-up in the course of the fourth follow-up year. The radiographies and special examinations done at TAUH were included in the number of radiological examinations, those done at other health care units were not included. The patients' performance status was checked at the last visit of each follow-up year. Survival was checked both for the first and last follow-up visit each follow-up year when describing the dependency of survival on length of follow-up.

The criteria for recurrence of cancer were the reappearance of a tumour after disappearance, either on the original site or as a metastasis. Recurrences of cancer were counted together cumulatively for the five follow-up years for the accrued number of follow-up years. The probability of recurrence was calculated separately for each follow-up year. For example, in the third follow-up year the recurrence probability of cancer seen in radiographies was the number of recurrences found in radiographies during the third follow-up year divided by the entire number of patients at the beginning of the year subtracted half of the patients who left the follow-up during the year (dead, left for other reasons, recurrence found through other methods). The probability of non-recurrence was calculated by subtracting the probability of recurrence from 100%. The cumulative risk of recurrence was calculated by multiplying the probability of non-recurrence of current year and the previous cumulative probability and subtracting the product from 100%. On the same principle the probability of survival was calculated.

Follow-up events before the date of confirmation of those experiencing a recurrence of cancer likewise patients in whom a second cancer was found were counted together with the events of the patients only in the follow-up by follow-up year.

The events in follow-up after the date of confirmation of patients with recurrence of cancer were added to those follow-up events diagnosed in patients whose disease had remained metastatic throughout.

The information contained in the questionnaires was stored as a Paradox database at the University of Tampere Computer Centre. For the statistical analyses BMDP (1990) sofware program was used. The findings were analysed by randomised arms. Cumulative recurrence and survival probabilities were calculated by actuarial estimates from life tables. The equality of cumulative recurrence and survival curves was tested using Wilcoxon (Gehan) statistics. Distributions are presented principally in cross-tabulations. Differences in distributions were tested using Chi-square test. The level of statistical significance was set at $p < 0.05$.

5 Results

5.1 Success of randomisation

The data included a total of 869 cancer patients. Of these 452 were in the double-reading arm and 417 in the single-reading arm. There was no statistically significant difference between the arms regarding sex, confirmation of cancer diagnosis, size of tumour, type of disease, primary treatment and response to it and patient's performance status at the end of primary treatment. More metastasized cancers were found in the double-reading arm than in the single-reading arm. No difference was found in the men's age distribution. There was a difference between the arms for women's age distribution. In the single-reading arm the percentage proportion of women aged 45–54 is higher in comparison with the double-reading arm, and in the double-reading arm the percentage proportion of women aged 75–84 is higher compared to the single-reading arm.

5.1.1 Numbers, sex and age

The study included 869 patients. Of these 452 (52.0%) were in the double-reading arm and 417 (48.0%) were in the single reading arm. The difference in size between the arms was 35 patients. The basis for randomisation was the day of birth, i.e. those born on an odd-numbered day were randomised to the double-reading arm and those born on an even-numbered day were randomised to the single-reading arm. In a year there are seven more odd-numbered days than even-numbered days, thus it was assumed that the discrepancy in size between the arms would be approximately 20.

There were 657 (75.6%) women and 212 men (24.4%) in the data as a whole. The proportion of women was greater than men in each arm, in the double-reading arm 74.1% were women and in the single-reading arm 77.2% were women. No statistically significant difference between the arms in the proportions of women and men was noted (p=0.29) (Table 1).

The average age of the patients was 58.7 years (range 21–94) in the data as a whole. In the double-reading arm the average age of patients was 59.0 years and 58.3 years in the single-reading arm. In the data as a whole, women's average age was 57.8 years (range 24–94) and men's average age was 61.4 years (range 21–85). Statistically significant difference between the arms in the age of women (p=0.006), but not in men (p=0.83), was noted. The data included no juvenile patients because after treatment children's follow-up is not conducted at the Department of Oncology, but in the paediatric clinic (Table 1).

Table 1. Number (n) and distribution (%) of patients at the TAUH Department of Oncology in 1991–1997 by sex, age and research arm.

Age	Double-reading arm				Single-reading arm			
	Men		Women			Men		Women
	n	%	n	%	n	%	n	%
21–44	15	12.8	52	15.5	11	11.6	43	13.4
45–54	17	14.5	83	24.8	12	12.6	94	29.2
55–64	28	23.9	86	25.7	18	18.9	87	27.0
65–74	43	36.8	61	18.2	44	46.3	75	23.3
75–84	13	11.1	48	14.3	9	9.5	18	5.6
85–94	1	0.9	5	1.5	1	1.1	5	1.5
Total	117	100. 0	335	100. 0	95	100.0	322	100.0

5.1.2 Primary site, cancer confirmation and size of tumour

Breast cancer was the most common cancer (59.4%) in the data as a whole and in each respective research arm (59.1% / 59.7%) (Table 2). This also explains the larger proportion of women in the patient data as a whole. In the period 1991–1995 the number of new cases of breast cancer diagnosed was 15.0% of all new cancer cases and 28.2% of new cancer cases in women for the entire country (Finnish Cancer Registry 1993, 1996, 1997). Of breast cancer cases in the data as a whole 7 (5/2) (1.4%) were diagnosed in men.

After breast cancer the next most common cancers to be diagnosed were lung cancer, lymphoma, and skin cancer, i.e. melanoma. Patients with these four types of cancer amounted to 805 (92.6%) of the data as a whole and in the double-reading arm they accounted for 93.0% and 92.4% in the single-reading arm (Table 2). The types of cancer occurring in the data are well representative of the arms of patients remaining in follow-up at the Department of Oncology, but otherwise represent only a fraction of all the types of cancer. The majority of patients with breast cancer, lung cancer, lymphoma, melanoma and thyroid cancer remain in follow-up at the TAUH Department of Oncology after primary treatment. Patients with otorhinolaryngological, urological, neurological and gynaecological cancers do not remain with the TAUH Department of Oncology for follow-up even though they have received primary treatment at this clinic. Follow-up for these patients is arranged in the respective clinics of each speciality.

Table 2. Number of cancers (n) and distribution (%) of patients at the TAUH Department of Oncology in 1991–1997 by primary site of tumours and research arm.

Primary site	Double-reading arm		Single-reading arm	
	n	%	n	%
Breast	267	59.1	249	59.7
Lung	59	13.1	47	11.3
Lymphoma	51	11.3	44	10.6
Skin	43	9.5	45	10.8
Thyroid	16	3.5	16	3.8
Other	16	3.5	16	3.8
Total	452	100.0	417	100.0

The cancer diagnosis of a tumour was confirmed histologically for 840 patients (96.7%) in the data as a whole, and no difference between the arms was noted (96.5%/ 96.9%). For a total of 29 patients (3.3%) the diagnosis was confirmed cytologically.

In 751 patients (86.4%) it was possible to measure the size of the tumour. In the double-reading arm tumours in 87.0% of patients could be measured and in the single-reading arm tumours of 86.0% of patients could be measured. There was a total of 118 patients (13.6%) for whom the size of tumour could not be measured. The size of the primary tumour was 26.9 mm on average (variation 2–200 mm) in the data as a whole with no difference noted between the arms (27.5 mm / 26.3 mm).

The size of the tumour was determined histologically for 307 patients (40.9%) of all measurable tumours. Tumour size in the double-reading arm was measured histologically for 38.9% of patients and in the single-reading arm for 43.0% of patients. The size of breast cancers was measured histologically for 50.4% of patients in the double-reading arm and for 58.0% of patients in the single-reading arm. In surgery the size of the tumour was determined for 233 patients (31.0%) of all measurable tumours. In the double-reading arm the size of the tumour was determined in surgery for 33.6% and in the single-reading arm for 27.5%. Tumour size was determined radiologically for 183 patients (24.4%) of all measurable tumours and no difference between the arms was noted (24.4% / 24.3%).

5.1.3 Stage of disease

In the data as a whole there were 484 (62.5%) local cancers. Patients in the double-reading arm had a total of 237 (59.1%) and in the single-reading arm 247 (66.2%) local cancers. The number of local tumours in the single-reading arm was statistically significantly larger than in the double-reading arm (p=0.041) (Table 3). Lymphomas

were addressed in a group of their own. In both arms the most common disease was local breast cancer. Among the breast cancer patients in the double-reading arm there were 163 (61.0%) local cancers and in the single-reading arm 172 (69.1%). The cancer had not disseminated or this had not been suspected before commencing primary treatment. Both arms included more local melanoma tumours than disseminated melanomas.

In lung cancer patients the disease was non-localized in 52.5% of cases in the double-reading arm and 48.9% of cases in the single-reading arm. Breast cancers with regional lymph nodes positive amounted to 96 (36.0%) in the double-reading arm and 73 (29.3%) in the single-reading arm. Breast cancers which had disseminated elsewhere in the body were found in 3.0% / 1.6% in respective arms. Each arm contained 5 patients with bilateral breast cancer. The stage was known for 99.3% of patients before commencement of primary treatment in the data as a whole and no difference between the arms was found (99.1% / 99.5%) (Table 3).

Patients with lymphoma amounted to 95 in the data as a whole, with 53.7% of them in the double-reading arm. In each arm stage I–II tumours were the most common (70.6%/ 70.4%). In the double-reading arm there were 13.7% and in the single-reading arm 18.2% of patients with stage III of cancer. The corresponding figures for stage IV were 15.7% and 11.4% respectively.

In the data as a whole there were 25 patients with a second primary cancer, but at the time of providing primary treatment for the present cancer there had been no signs of the previous cancer. The double-reading arm contained 11 such patients and the single-reading arm 14.

Table 3. Number (n) and proportion (%) of patients with localized cancer per cancer type at the TAUH Department of Oncology in 1991–1997 by site of primary tumour and research arm.

Primary site	Double-reading arm		Single-reading arm	
	n	%	n	%
Breast	163	61.0	172	69.1
Lung	22	37.3	18	38.3
Skin	37	86.0	44	97.8
Thyroid	13	81.3	11	68.8
Other	2	12.5	2	12.5
Total	237	59.1	247	66.2

5.1.4 Primary treatment and response

Primary treatment had been surgery, radiation or drug treatment or various combinations of these. In the double-reading arm 67.3% of patients had received combined treatments, in the single-reading arm 62.3%. The most common combination of treatments was surgery with radiation treatment in both arms. Surgery was the most common single treatment in both research arms. In the data as a whole 7 patients had not received any treatment (Table 4).

In the double-reading arm a complete response to treatment was achieved in 73.7% of patients and in the single-reading arm 76.3%. In 3.9% of patients in the double-reading arm and in 2.4% of patients in the single-reading arm treatment did not bring about a change in the tumour or the disease progressed in spite of treatment. For 17.3% of all patients the response to primary treatment was not known or it was not measurable at the time the treatment was ended. No statistically significant difference between the arms in the response to primary treatment was noted (p=0.40) (Table 5).

Table 4. Number (n) and distribution (%) of patients at the TAUH Department of Oncology in 1991–1997 by primary treatment and research arm.

Primary treatment	Double-reading arm		Single-reading arm	
	n	%	n	%
Surgery	105	23.2	116	27.9
Surgery and radiotherapy	122	27.0	121	29.0
Surgery, radiotherapy and/or drug treatment	159	35.2	123	29.5
Radiotherapy and/or drug treatment	60	13.3	56	13.4
No treatment	6	1.3	1	0.2
Total	452	100.0	417	100.0

Table 5. Number (n) and distribution (%) of patients at the TAUH Department of Oncology in 1991–1997 by response to primary treatment and research arm.

Response	Double-reading arm		Single-reading arm	
	n	%	n	%
Complete	333	73.7	318	76.3
Partial	22	4.9	18	4.3
No change	11	2.4	5	1.2
Progressive	7	1.5	5	1.2
Not measurable	3	0.7	0	0.0
Not known	76	16.8	71	17.0
Total	452	100.0	417	100.0

5.1.5 Patients' performance status at the end of primary treatment

Patients' performance status at the end of primary treatment was good (Zubrod 0–1) in 93.6% of patients in the double-reading arm and 95.4% of patients in the single-reading arm. No patients were found in either arm who were completely immobile or incapable of taking care of themselves (Zubrod 4) at the beginning of follow-up. There was not a statistically significant difference in the performance status between the arms (p=0.27) (Table 6).

Table 6. Number (n) and distribution (%) of patients at the TAUH Department of Oncology in 1991–1997 by performance status after primary treatment and by research arm.

Performance status	Double-reading arm		Single-reading arm	
Zubrod	n	%	n	%
0	279	61.7	285	68.4
1	144	31.9	113	27.1
2	26	5.8	18	4.3
3	1	0.2	0	0.0
Not known	2	0.4	1	0.2
Total	452	100.0	417	100.0

5.2 Total material

The patients included in the study were undergoing follow-up at the TAUH Department of Oncology after primary treatment. The follow-up was accomplished during the period 1991–1997. Patients were followed-up both before recurrence of cancer and after this. Patients fell into three groups, firstly those patients who during the period of the study were only in follow-up after primary treatment and experienced no recurrence of the disease. Such patients numbered 530, which was 61.0% of all patients in the study. Of these 274 (60.6%) belonged to the double-reading arm and 256 (61.4%) belonged to the single-reading arm. Those patients in whom the disease recurred or in whom a totally new cancer was detected at some point in follow-up amounted to 246 (28.3%), of whom 124 (27.4%) in the double-reading arm and 122 (29.3%) in the single-reading arm. The third group consisted of those patients whose cancer remained metastatic after primary treatment and whose cancer did not improve during the period of the study. Such patients numbered 93, which was 10.7% of all patients in the study. Of the

patients whose cancers remained metastatic 54 (11.9%) belonged to the double-reading arm and 39 (9.4%) belonged to the single-reading arm.

The events of those patients who experienced a recurrence of cancer and those patients in whom another cancer was diagnosed during follow-up were added together before the date of confirmation of recurrence with the patients who were only in follow-up for each year. On the other hand the follow-up events after confirmation of patients who experienced a recurrence were added to the follow-up events of those who belonged to the group of patients whose cancers had remained metastatic.

A total of 8921 visits were made to the outpatient oncologic unit by all the patients included in the data. Of these 4695 (52.6%) were made by patients in the double-reading arm and 4226 (47.4%) were made by patients in the single-reading arm. The total follow-up years (patient-years) for the data as a whole was 2811, of which 1458 (51.9%) were by those in the double-reading arm and 1353 (48.1%) were by those in the single-reading arm. The total number of radiological examinations for the whole study population was 9656 during the first five years. Of these 4954 were made for patients in the double-reading arm, which was 51.3% of all examinations and in the single-reading arm respectively 4702 (48.7%). The distribution of the radiological examinations done on the whole patient population amounted to 5.5% of all examinations at the Department of Radiology during the period 1991–1997.

5.3 Non-recurrent phase of cancer

5.3.1 Visits of follow-up

The patients attended the outpatient unit either at times agreed in advance or spontaneously on extra visits. The total number of visits was 7055, of which 3630 (51.5%) in the double-reading arm and 3425 (48.5%) in the single-reading arm. The total number of follow-up years was 2366, of which 1205 (50.9%) among patients in the double-reading arm and 1161 (49.1%) in the single-reading arm.

In the double-reading arm the median follow-up time was 3 years, 2 months and 24 days (range 30 days – 5 years) and in the single-reading arm 3 years, 4 months and 27 days (range 28 days – 4 years, 11 months and 25 days). The difference between the two median follow-up times was 2 months and 3 days (Figure 1).

The average number of follow-up visits was 9.1 per patient and 3.0 per patient year. No difference was found between the arms in the overall distribution of follow-up visits either by patient or by follow-up years. In the first year of follow-up there were on average 4.0 visits per patient in the double-reading arm and 3.9 visits in the single-

reading arm. The average visits for the following years diminished in both arms. There was not a statistically significant difference between the arms in the average follow-up visits per patient year (p=0.78) (Figure 2).
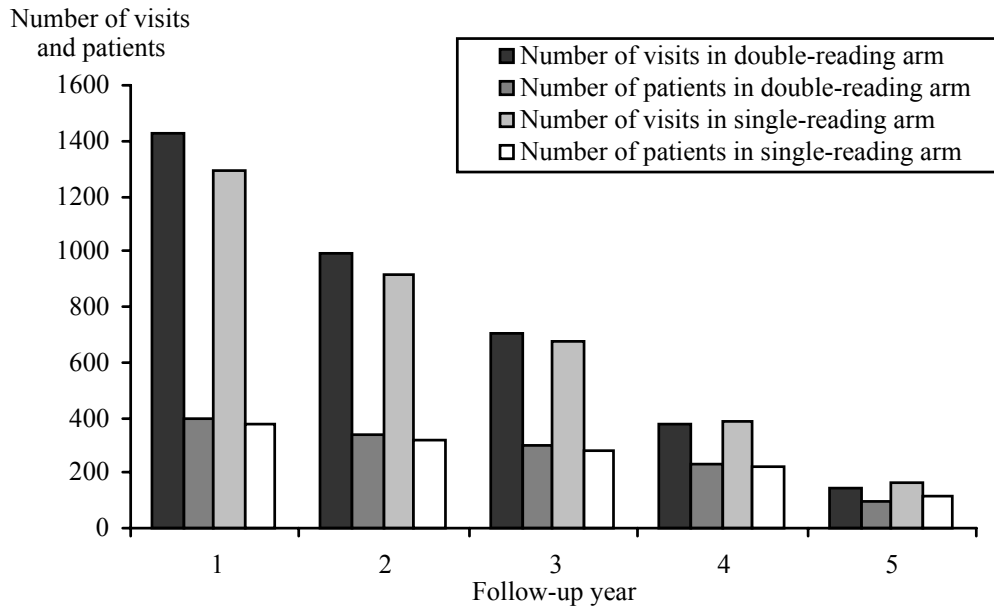
Figure 1. Number of patients and number of visits at the the TAUH Department of Oncology in 1991–1997 by year of follow-up and research arm.
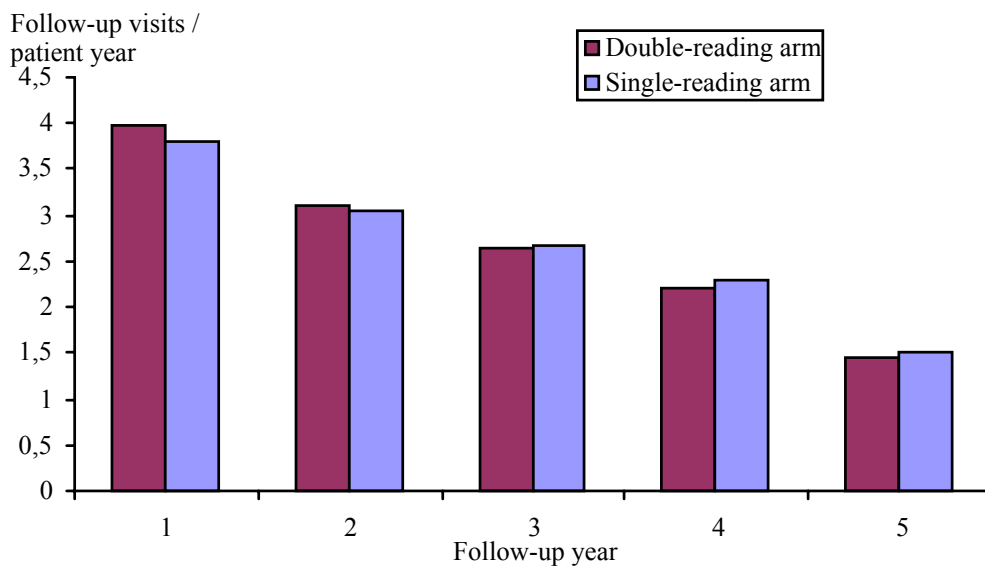
Figure 2. Follow-up visits per patient year at the TAUH Department of Oncology in 1991–1997 by year of follow-up and research arm.

5.3.2 Types of visit

A total of 6241 routine visits was made, i.e. 88.5% of all visits. Patients in the double-reading arm made 3220 visits, 51.6% of all routine visits made by patients included in the data. The total of routine visits made by patients in the single-reading arm was 3021 (48.4%). Routine visits per follow-up year in both research arms were highest in the first year of follow-up, no differences were found between the arms (3.3/3.2) (Figure 3).

There were no differences between the arms regarding routine visits and follow-up visits in general. In the data as a whole there were 814 extra follow-up visits, 11.5% of all follow-up visits made. Patients in the double-reading arm made 410 extra visits, which was 50.4% of extra visits in the data as a whole. In both research arms there were 0.6 extra visits per patient year in the first year of follow-up, which was more than in other follow-up years. The proportion of extra visits per follow-up year was greater in the single-reading arm in the three last years and the discrepancy appeared to increase as follow-up progressed. The number of extra visits in the single-reading arm was not statistically significantly larger than in the double-reading arm (p=0.10). In the fourth year of follow-up false suspicions of recurrence caused 50.0% of all extra visits. These false suspicions of recurrence were due to other reasons than the radiologist's actions. However, in the fifth year of follow-up radiologist's false suspicions of recurrence in special radiological examinations followed in 35.3% of all extra visits (Figure 4, note scaling).
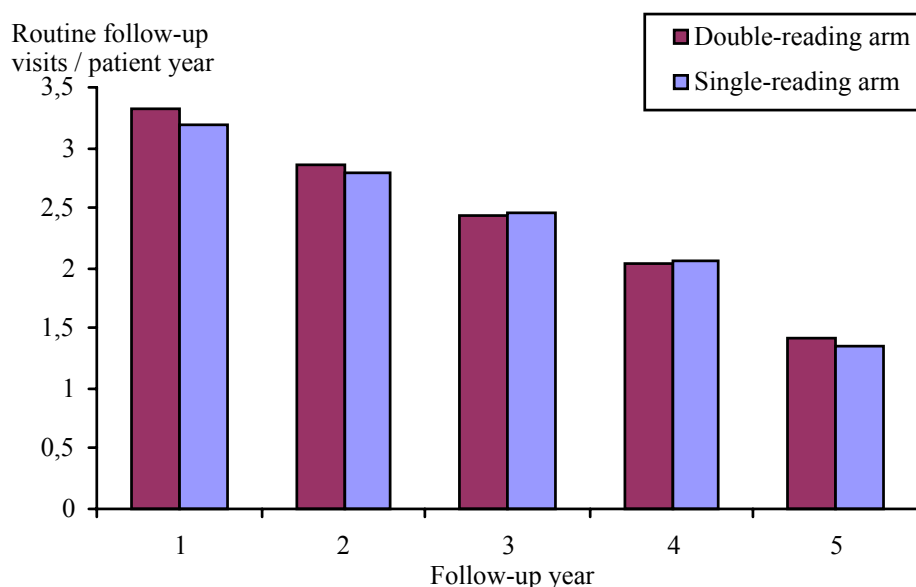

Figure 3. Routine visits per patient year at the TAUH Department of Oncology in 1991–1997 by year of follow-up and research arm.
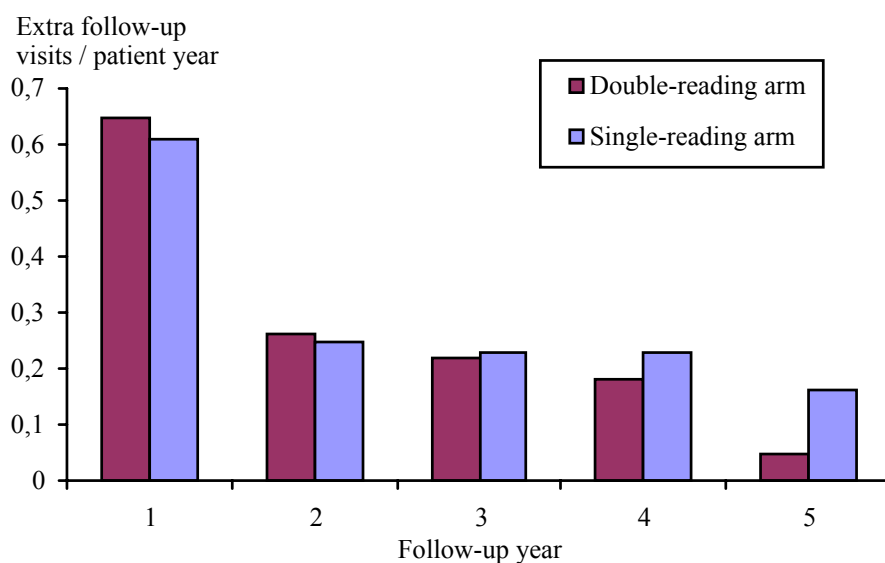
Figure 4. Extra follow-up visits per patient year at the TAUH Department of Oncology in 1991–1997 by year of follow-up and research arm.

Extra visits made due to the patient's request totalled 262, which was 3.7% of all visits. In the double-reading arm extra visits due to the patient's request accounted for 3.9% and in the single-reading arm 3.5%. In the double-reading arm follow-up visits at doctor's request amounted to 533, i.e. 7.6% of all visits. In the double reading arm extra visits at doctor's request totalled 260, which was 7.2% and in the single-reading arm 8.0%.

The finding in a radiological examination was the most common reason (54.0%) for extra follow-up visits requested by doctors. In the double-reading arm extra visits at doctor's request accounted for 55.8% and in the single reading arm for 52.4% of all extra visits made. About half of these visits were made during the first follow-up year in both arms, the most common finding being radiation treatment reaction in chest radiographies. In the single-reading arm in the fourth and fifth years extra visits were due to examinations to confirm suspected recurrences observed either primarily by special radiological examinations or by other methods. The difference of extra follow-up visits occasioned by radiological findings was not statistically significant between the arms (p=0.10) (Figure 5, note scaling).

The second most common reason for extra follow-up visits requested by a doctor were laboratory findings, in the double reading arm in 22.7% and in the single reading arm 24.4%. Status finding occasioned an extra follow-up visit requested by a doctor in 18.0% in the double-reading arm and 19.2% in the single reading arm.

Extra follow-up visits due to other reasons amounted to 19, which was 2.3% of all extra visits. The reason for a follow-up visit remained unclear for not a single patient in either arm.
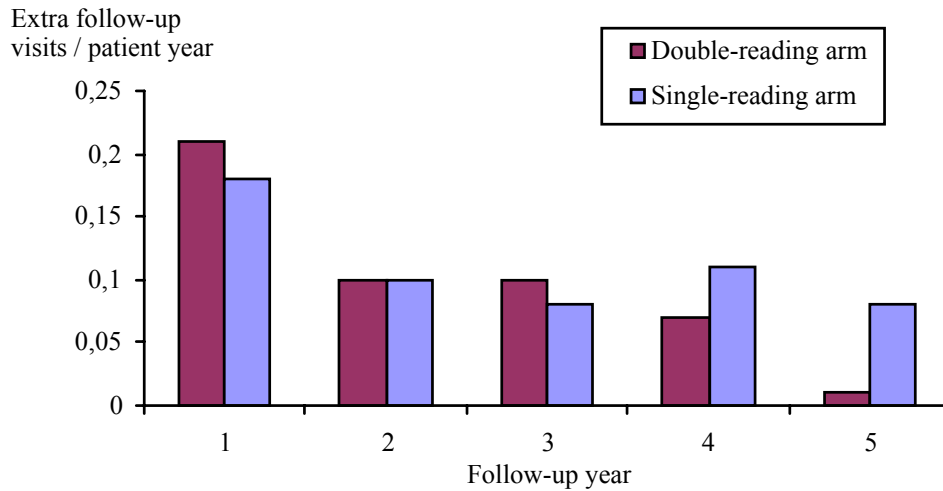
Figure 5. Extra follow-up visits occasioned by radiological findings per patient year at the TAUH Department of Oncology in 1991–1997 by year of follow-up and research arm.

5.3.3 Doctors in the outpatient clinic

In the entire period of the research there were 28 different doctors receiving patients in the Department of Oncology outpatient unit. They included 3 chief physicians, 8 oncologists, and 17 doctors in training. For follow-up visits the average number of doctors to one patient in one year of follow-up was 2 in each research arm (range 1–5 / 1–4). Double-reading arm patients in follow-up for 2 years had on average 1 more doctor for follow-up visits than those in the single-reading arm, but thereafter no difference was found for patients in follow-up (Figure 6).
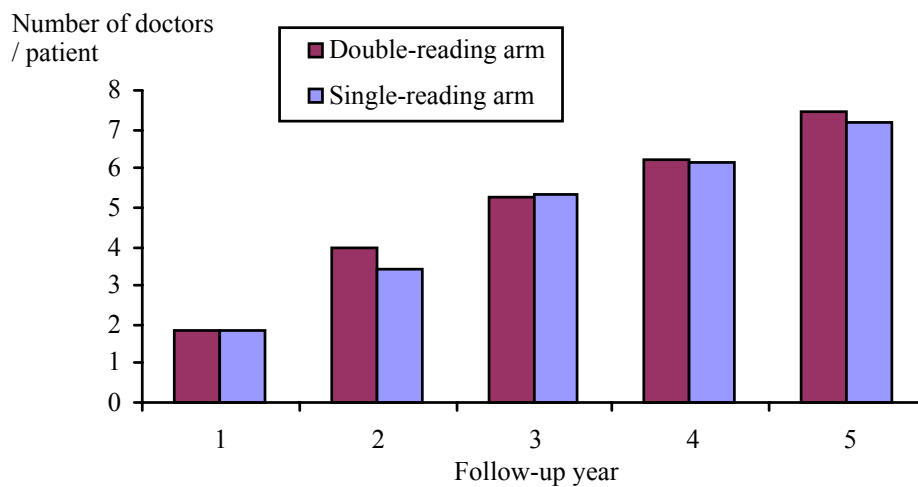

Figure 6. Cumulative number of doctors per patient at the TAUH Department of Oncology in 1991–1997 by year of follow-up and research arm.
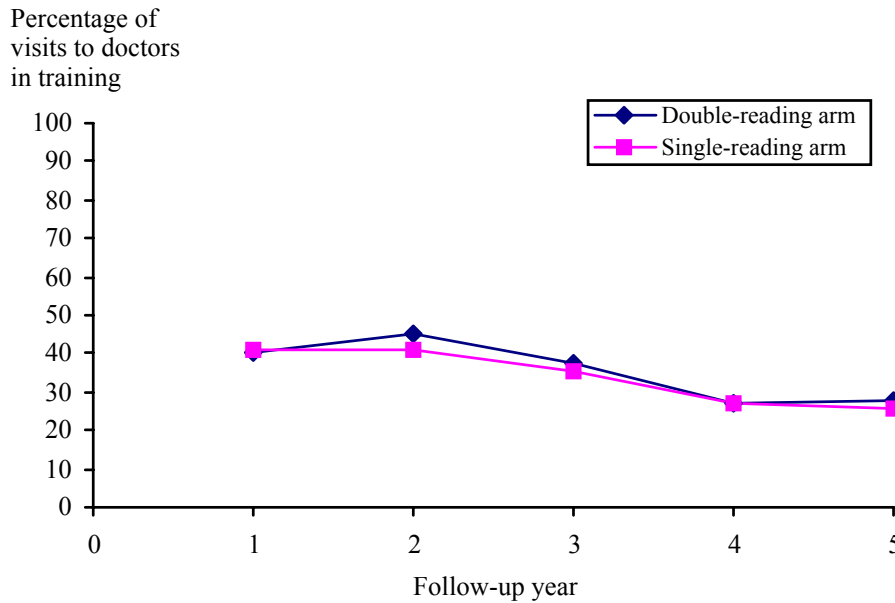
Figure 7. Proportion (%) of visits to doctors in training among all visits to doctors at the TAUH Department of Oncology in 1991–1997 by year of follow-up and research arm.

Follow-up visits made to doctors in training amounted to 2726 (38.6%) of the entire data. Visits made by patients in the double-reading arm amounted to 39.4% and by patients in the single-reading arm to 37.8% in all years. Follow-up visits made to specialists amounted to 4156 (58.9%), with no differences found between the arms (58.3% / 59.5%). Follow-up visits made to chief physicians amounted to 173 (2.5%) of all follow-up visits and no differences were found between the arms (2.3% / 2.7%). No differences were found between the arms during follow-up for numbers of doctors in training and specialists per patient. In each year of follow-up more visits were made to specialists than to doctors in training (Figure 7).

5.3.4 Number of radiological examinations

In the first five years a total of 6636 radiological examinations were done on the entire patient population. Of these 3344 (50.4%) were on patients in the double-reading arm and 3292 (49.6%) were on patients in the single-reading arm. In the first two years of follow-up a higher percentage of radiological examinations was done on patients in the double-reading arm than in the single-reading arm, approximately proportional to the number of patients in each arm. In the third and fourth year the number of examinations was higher in the single-reading arm (Figure 8).
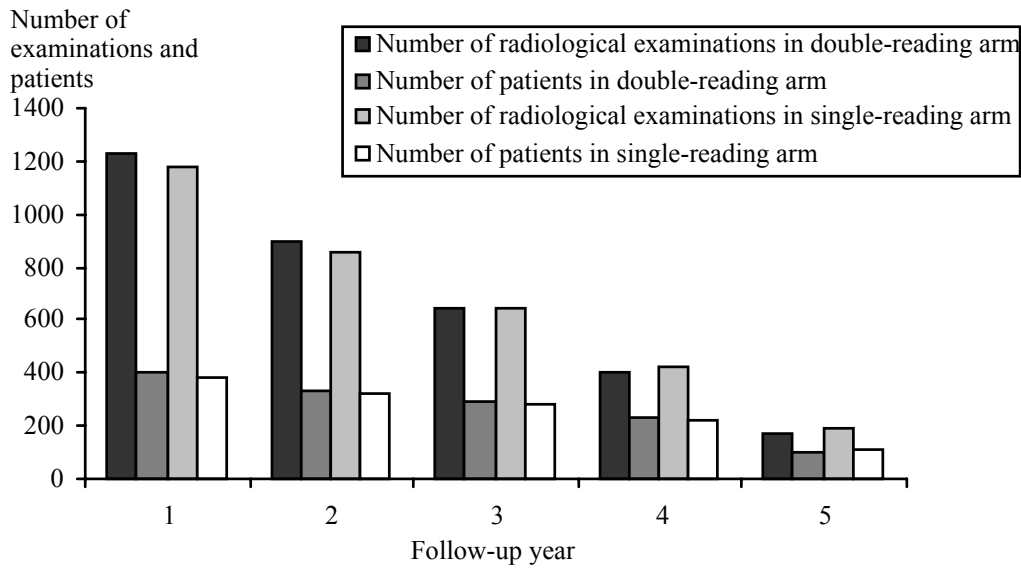
Figure 8. Number of patients and number of radiological examinations at the TAUH Department of Oncology in 1991–1997 by year of follow-up and research arm.
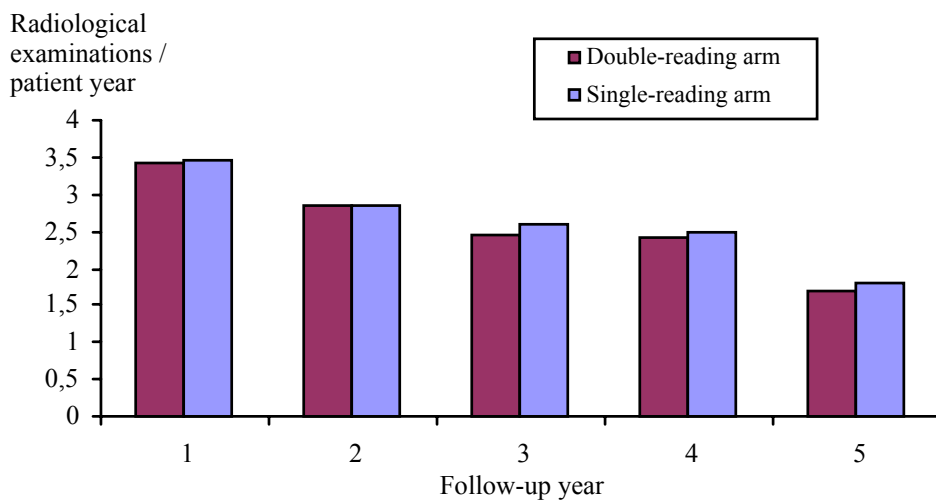

Figure 9. Radiological examinations per patient year at the TAUH Department of Oncology in 1991–1997 by year of follow-up and research arm.

In the data as a whole 8.6 examinations were done per patient and 2.8 examinations per year of follow-up. Examinations done on patients in the double-reading arm amounted to 8.4 per patient and in the single-reading arm 8.7 per patient. In the first year 3.4 radiological examinations were done per year of follow-up for patients in the double-reading arm and 3.5 examinations for patients in the single-reading arm. In the following years the numbers of examinations diminished per year of follow-up in both arms. The number of examinations per patient year in the single-reading arm was not statistically significantly larger than in the double-reading arm (p=0.81)(Figure 9).

5.3.5 Types of radiological examinations

Of all the radiological examinations made, 4356 were routine (65.6%). In the double-reading arm there were 2195 routine examinations (65.6%) and in the single-reading arm 2161 (65.6%). In the two first years of follow-up there were 2 routine examinations per patient year and in the fifth year an average of 1 (Figure 10). Routine examinations of all were in the same relation in both research arms and no differences were found during follow-up.

The extra examinations were made principally for two reasons, firstly because of suspected recurrence of cancer and secondly because of negative effects of primary treatment. A total of 580 (8.7%) extra examinations in the data as a whole were made because of suspected recurrence of cancer, of which 284 (8.5%) in the double-reading arm and 296 (9.0%) in the single-reading arm. Uncertain finding caused 496 (7.5%) examinations to be made within the data as a whole, of which 262 (7.8%) in the double-reading arm and 234 (7.1%) in the single-reading arm. For the data as a whole possible side effects of treatment caused 100 (1.5%) examinations, and no difference between the arms was found (1.6%/1.4%). In both research arms the examinations due to side effects of treatment concentrated on the first two years of follow-up. In the data as a whole a total of 160 extra examinations, which was 2.4% of the total number in the research was done for other reasons. A reason not connected to cancer caused 274 examinations, 4.1% of the entire data, and no differences between arms were found.

Some of the radiological examinations connected to follow-up were made at the request of the Department of Oncology ward when for one reason or another a patient had been admitted to hospital as an in-patient. Such examinations amounted to 34, of which 19 were for patients in the double-reading arm and 15 for patients in the single-reading arm. Radiological examinations requested by another doctor amounted to 636, which was 9.6% of all. In the double-reading arm some other doctor requested 9.0% and in the single-reading arm 10.1% of all radiological examinations and in both arms 76.0% of those made for a reason not connected to cancer.
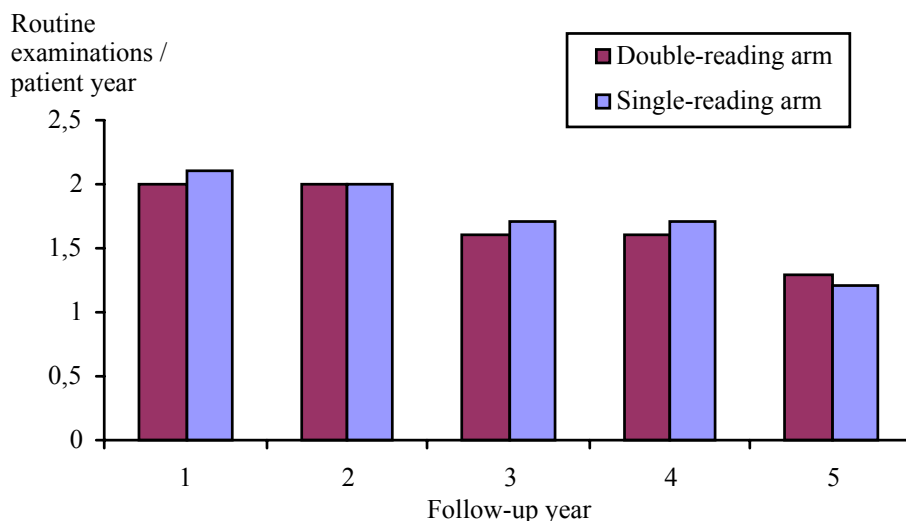
Figure 10. Routine radiological examinations per patient year at the TAUH Department of Oncology in 1991–1997 by year of follow-up and research arm.

5.3.6 Plain radiography

A total of 4351 plain radiographies were done for the entire population of the study, which was 65.6% of all radiological examinations. The number of radiographies for the double-reading arm patients was 2207, which was 66.0% of all examinations in the arm. In the single-reading arm the number of radiographies was 2144, which was 65.1% of all examinations. In the data as a whole an average of 5.6 radiographies was made for each patient, 1.8 for each year of follow-up. Radiographies made for patients in the double-reading arm amounted to 5.5 per patient and in the single-reading arm 5.7 per patient. In the first year of follow-up 2.5 radiographies were made per patient in the double-reading arm and 2.3 in the single-reading arm. In the following years the number of radiographies per patient year diminished in both arms. No statistically significant difference between the arms in the number of plain radiographies was noted (p=0.20) (Figure 11).

No differences were found in the total numbers of radiographies between the randomised arms, nor did any differences occur during follow-up years. The most common radiograph was of the chest. That type amounted to 3705, which was 55.8% of all radiological examinations and 85.2% of all plain radiographies. Of the patients in follow-up included in the study the number of chest radiographies was 10.1% of all the chest radiographies made at the Department of Radiology and 4.0% of all radiological examinations in the course of follow-up. Among patients in the double-reading arm chest radiographies amounted to 86.0% of all radiographies and in the single-reading arm 84.3%. In each research arm 4.8 chest radiographies per patient were made. In each research arm 1.6 chest radiographies were made per year of follow-up. For each arm most chest radiographies were made in the first year of follow-up compared to other years. No statistically significant difference between the arms in the number of chest

radiographies (p=0.14) was noted (Figure 12). After chest radiographies the most common were spine and limb radiographies (Table 7).
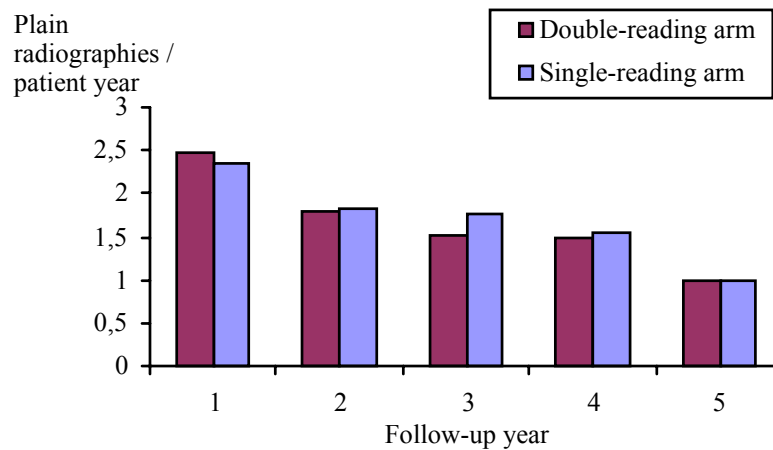

Figure 11. Plain radiographies per patient year at the TAUH Department of Oncology in 1991–1997 by year of follow-up and research arm.
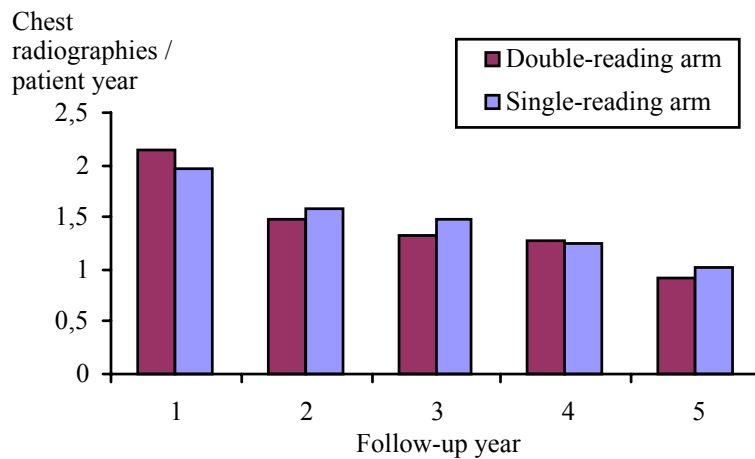

Figure 12. Chest radiograhphies per patient year at the TAUH Department of Oncology in 1991–1997 by year of follow-up and research arm.

Table 7. Site of plain radiographies quantitatively (n) and percentually (%) of patients at the TAUH Department of Oncology in 1991–1997 by year of follow-up and research arm.

Plain radiography	Double-reading arm		Single-reading arm	
	n	%	n	%
Lung	1897	86.0	1808	84.3
Spine	82	3.7	97	4.5
Upper limb	51	2.3	62	3.0
Pelvis	27	1.2	24	1.1
Lower limb	95	4.3	75	3.5
Ribs	15	0.7	39	1.8
Other	40	1.8	39	1.8
Total	2207	100.0	2144	100.0

5.3.7 Doctors at the Department of Radiology

The total number of radiologists interpreting plain radiographies during the entire period of the study was 20. These comprised 1 chief physician, 6 radiologists and 13 doctors in training. During the first five years there was on average a larger number of specialists per patient in the double-reading arm than in the single-reading arm compared to the number of doctors in training. The radiographies of patients in the double-reading arm in the first year of follow-up were interpreted on average by 1 radiologist. The radiographies of patients followed up for 2 to 4 years were interpreted on average by 3 different radiologists. The radiographies of patients followed up for 5 years were interpreted by 4 radiologists. Radiographies of patients in the single-reading arm were interpreted on average by 1 radiologist in the first year, patients in follow-up for 2 to 3 years and longer were interpreted on average by 2 radiologists.

5.3.8 Need for a statement by a radiologist

In the single-reading arm a total of 2144 plain radiographies were made. Of these 1927 (89.9%) were examinations requested via the Department of Oncology, and 217 requested by some other doctor. An oncologist requested a separate statement from a radiologist on 44.4% (856) of all the examinations done for the Department of Oncology. In the first year in the single-reading arm statements from a radiologist were requested on 40.6% of all radiographies. In the following years the need for statements increased (Table 8). Those patients of the single-reading arm on whose radiographies the clinician had never requested a radiologist's statement amounted to 29 (7.7%). At least one statement was requested on the radiographies of patients with lymphoma at some point during follow-up. In the double-reading arm, separate statements were requested on 128 plain radiographies, 6.4 % of all radiographies, even though statements were issued in any case without need for a separate request.

In the single-reading arm 1808 chest radiographies were made of which 1686 (93.3%) at the request of the Department of Oncology and 122 at the request of some other doctor. The oncologist separately requested a radiologist's statement on 661 chest radiographies, which was 39.2% of all chest radiographies done for cancers. In the second and fifth years more radiologist's statements were requested compared to other years (Table 9). Of all radiographies for which a statement was requested 45.2% were requested by 4 clinicians, one of these being a doctor in training and the others specialists.

For the chest radiographies of the patients in the double-reading arm statements were separately requested for 6.3%.

Table 8. Number of all plain radiographies (n) on which a radiologist's statement was requested separately and their percentual (%) proportion of patients at the TAUH Department of Oncology in 1991–1997 by year of follow-up and single-reading arm.

Year of follow-up	Single-reading arm		Total
	n	%	
1	297	40.6	731
2	234	48.4	483
3	167	42.5	393
4	107	47.6	225
5	51	53.7	95
Total	856	44.4	1927

Table 9. Number of chest radiographies (n) on which a radiologist's statement was requested and their percentual proportion (%) of total chest radiographies made by the TAUH Department of Oncology in 1991–1997 by year of follow-up and single-reading arm.

Year of follow-up	Single-reading arm		Total
	n	%	
1	237	37.3	635
2	186	43.5	428
3	126	35.6	354
4	77	40.7	189
5	35	43.8	80
Total	661	39.2	1686

The savings in radiologist's work in the single-reading arm amounted to 55.6%, and this saving appeared to be independent of year or location of primary tumour. The ratio of the requests by doctors in training for statements to number of visits for the entire duration of follow-up was 0.23 (301/1297), the corresponding figure for specialists being 0.17 (360/2128). The need for statements among doctors in training in relation to number of visits increased throughout the first four years and was greater than that of specialists. In the fourth year a request for the radiologist's statement on a chest radiography was made for every third visit to a doctor in training (36/104). In two cases in these radiographies a doctor in training incorrectly suspected a recurrence of cancer and in one plain radiography the radiologist incorrectly suspected a recurrence of cancer. Other requests by doctors in training for a radiologist's statement involved no suspicion of recurrence. In the fifth year the need for statements among specialists in relation to number of visits was greatest compared to other years. When the patient's follow-up ended at the Department of Oncology the specialist wished to confirm the interpretation with the radiologist (Figure 13).
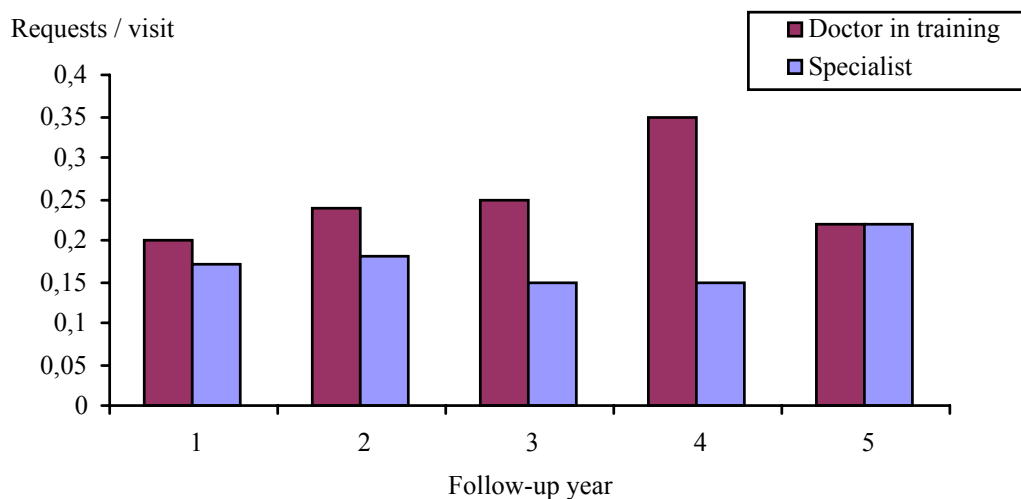
Figure 13. Number of requests for statements by doctors in training and by oncologists per visit at the TAUH Department of Oncology in 1991–1997 by year of follow-up among patients in the single-reading arm.

Table 10. Number (n) of single-reading arm patients' bone radiographies on which the clinician separately requested a radiologist's statement and their percentual distribution (%) of all bone radiographies made at the Department of Oncology in 1991–1997.

Plain radiography	Single-reading arm		Total bone radiographies
	n	%	
Spine	72	89.9	81
Upper limb	31	77.5	40
Pelvis	18	81.8	22
Lower limb	27	61.4	44
Ribs	33	89.2	37
Other	14	82.4	17
Total	195		241

In the first year a statement was requested by the cancer ward on 9 chest radiographies, and 7 of these came from specialists. In the single-reading arm radiologist's statements were separately requested on 195 bone radiographies, which was 10.1% of all plain radiographies in the arm and 80.9% of all bone examinations (Table 10). In the double-reading arm a radiologist's statement was separately requested on 13.3% of all examinations even though a statement had been provided without request.

Doctors in training had requested 47.7% and oncologists 52.3% of all radiologist's statements on bone radiographies. It emerged from the medical histories that the clinician had visited the radiologist for consultation on plain radiographies on ten occasions for patients in the double-reading arm and 8 times for patients in the single-reading arm.

5.3.9 Special radiological examinations

Of all radiological examinations 2285 (34.4%) were special examinations. Of these 1137 (34.0%) were made for patients in the double-reading arm and 1148 (34.9%) in the single-reading arm. The most common special examinations in both arms were mammographies and ultrasound examinations. For 99.0% breast ultrasound was combined with mammography in the double-reading arm and for 95.0% in the single-reading arm. Almost as many ultrasound examinations of the abdomen were done in both research arms. MRI examinations were done for 1.0% of patients in both arms (Table 11). The number of special examinations per patient was generally higher during the first two years of follow-up than during the following years in both arms. No statistically significant difference between the arms in the number of special radiological examinations per patient year (p=0.079) was noted (Figure 14).

Table 11. Number of special radiological examinations (n) and their percentual distribution (%) in the follow-up of patients at the TAUH Department of Oncology in 1991–1997 by research arm.

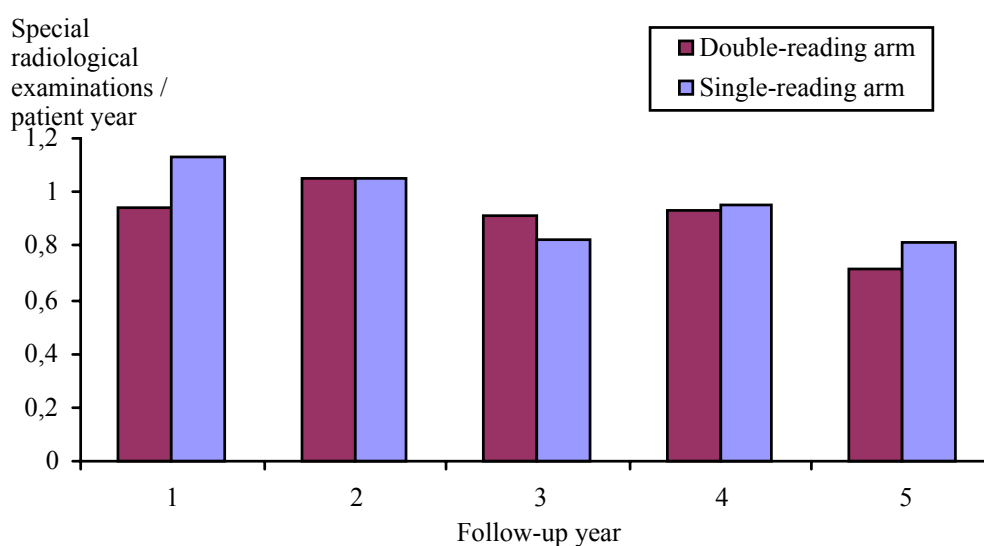| Examination	Double-reading arm		Single-reading arm	
	n	%	n	%
Mammography	389	34.2	387	33.7
Breast ultrasound	207	18.2	208	18.2
Other ultrasound	381	33.5	387	33.7
CT	82	7.2	78	6.8
MRI	11	1.0	12	1.0
Other	67	5.9	76	6.6
Total	1137	100.0	1148	100.0

Figure 14. Special radiological examinations per patient year at the TAUH Department of Oncology in 1991–1997 by year of follow-up and research arm.

A total of 27 special examinations were done due to inconclusive plain radiograph findings, of which 11 for patients in the double-reading arm and 16 for patients in the single-reading arm. In the double-reading arm 73.0% of special examinations in the first two years were done to confirm plain radiograph findings, in the single-reading arm the corresponding figure was 75.0%. The most common special examination in both arms was linear tomography. No MRI examinations were done in either arm to confirm inconclusive radiograph findings.

5.4 Recurrences and new cancers

In follow-up recurrences of cancer are searched for, which may present as local residives or metastases. It is also possible to find a completely different cancer. The clinician seeks recurrences in the patient above all through clinical examination, for example local residive in the treated breast of a breast cancer patient or new cancer in the contralateral breast. Symptoms described by the patient may indicate a possible recurrence of the disease. The clinician frequently requests laboratory or radiological examinations to further investigate a suspicion of recurrence. In radiographies the radiologist looks for local recurrences of cancer, for example in lung cancer or lymphomas, and for metastases, for example in breast cancer. In both randomised research arms there were about 3500 follow-up visits and a recurrence of cancer or a new cancer was found at every 30th visit. A recurrence of cancer was diagnosed in 227 patients, which was 29.3% of the data as a whole. In double-reading arm patients a recurrence occurred in 114 (28.6%) and in single-reading arm patients in 113 (29.9%). A totally new cancer was found in 10 (2.5%) patients in the double-reading arm and in 9 (2.4%) patients in the single-reading arm. In both arms more recurrences were found in the first year compared to other years. In the first three years 83.3% of all recurrences were found in the double-reading arm and 77.9% of all recurrences in the single-reading arm. In both research arms recurrences of cancer were found in all years of follow-up (Table 12). The differences of recurrence numbers by organ were not statistically significant between the arms (p= 0.64). Three (2/1) patients returned to the Department of Oncology after the end of follow-up for treatment of a recurrence of cancer. These recurrences have not been included in the recurrences of the arms.

Breast cancer recurred in 22.4% of all breast cancers in the double-reading arm and in 24.1% of those in the single-reading arm. There was no statistically significant difference of recurrence number by organ between the arms (p=0.64) (Figure 15). Totally new cancers were found in 9 breast cancer patients in the double-reading arm and in 6 patients in the single reading arm, more than other cancers.

In both research arms the cumulative recurrences during follow-up were the same There was no statistically significant difference (p=0.85) between the arms in the cumulative probability of recurrence (Figure 16).

Table 12. Number (n) of recurrences of cancer and their cumulative percentual (%) distribution of all recurrences of patients at the TAUH Department of Oncology in 1991–1997 by year of follow-up and research arm.

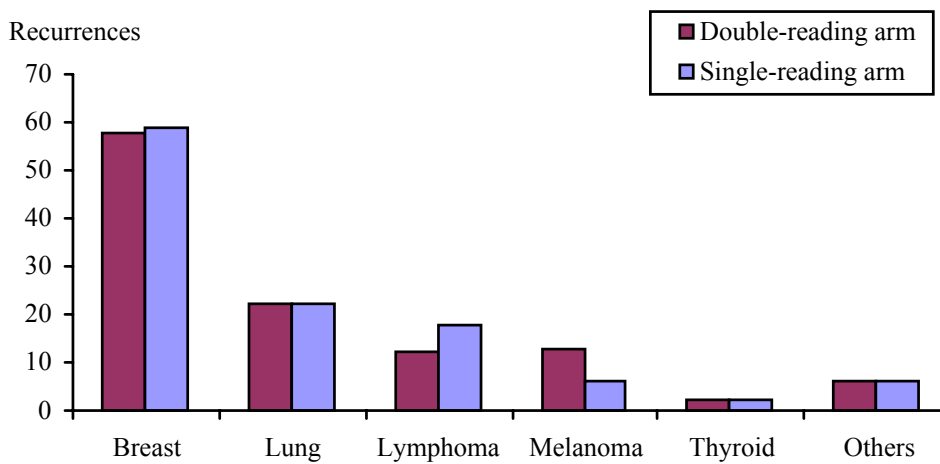| Year of follow-up	Double-reading arm			Single-reading arm		
	n (n = 114)	Cumul.%	Total	n (n = 113)	Cumul.%	Total
1	46	40.4	398	47	41.6	378
2	29	65.8	338	29	67.3	320
3	20	83.3	295	12	77.9	279
4	16	97.4	235	18	93.8	222
5	3	100.0	100	7	100.0	113

Figure 15. Recurrences of cancers in patients at the TAUH Department of Oncology in 1991–1997 by primary site and research arm.
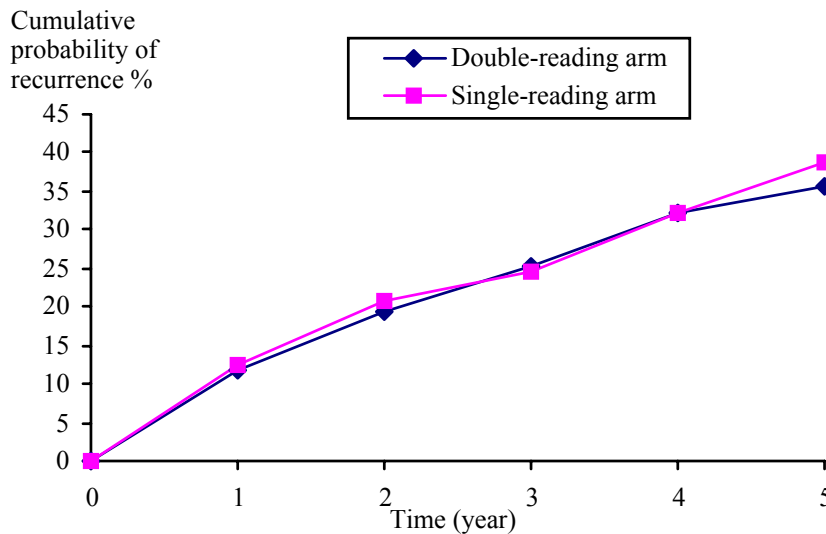

Figure 16. Cumulative probability (%) of recurrence of cancer in patients at the TAUH Department of Oncology in 1991–1997 by year of follow-up and research arm.

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5.4.1 Malignant lesions in plain radiography

Recurrence of cancer was found in plain radiographies in 55 patients (7.1%) of all patients and in 24.2% of all recurrences. Recurrences found by radiograph amounted to 49.1% among patients in the double-reading arm and to 50.9% in the single-reading arm. During the first two years of follow-up 74.5% of all recurrences were detected (74.1%/75.0%). In the fifth year of follow-up one recurrence of cancer was detected in the double-reading arm (Figure 17).

In the double-reading arm, whose radiographies were interpreted first by a clinician and next by a radiologist, each separately, 27 recurrences of cancer were detected. A clinician was the first to see these in 13 (48.2%), a radiologist in 11 (40.7%) and some other doctor in 3 (11.1%). Of recurrences found by clinicians 61.5% were found by doctors in training. All the recurrences found by radiologists were found by specialists. Findings of recurrences by clinicians and radiologists were distributed over all follow-up years. Recurrences found by other doctors were concentrated on the first year of follow-up.

In the single-reading arm, whose radiographies were interpreted only by a clinician, and by a radiologist only at a separate request, 28 recurrences of cancer and one totally new cancer were diagnosed. There were 13 (46.4%) recurrences found by clinicians, 53.8% of them doctors in training. A radiologist provided statements on request and diagnosed 8 (28.6%) recurrences, 3 (37.5%) of these by doctors in training. The information in the medical histories does not show a clear suspicion of cancer on the part of the clinician regarding these patients, at any rate she or he has for one reason or another wished to confirm the situation with a radiologist. Of all the recurrences in the arm 7 (25.0%) were found by some other doctor. The recurrence detections made by other doctors were mostly located in bones which are not radiographed routinely and would not have been detected without symptoms. Therefore the difference (3/7) is not connected with the setting of the study.
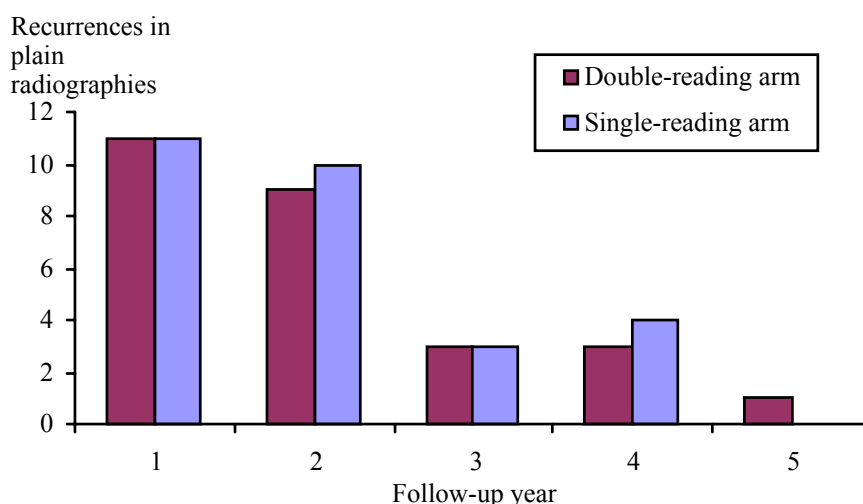

Figure 17. Number of recurrences found in plain radiographies among patients at the TAUH Department of Oncology in 1991–1997 by year of follow-up and research arm.

Recurrence of cancer was falsely suspected in 58 patients, which was 7.5% of all patients in follow-up. There were two patients in the double-reading arm who were twice falsely suspected of having a recurrence of cancer and one in the single-reading arm. For others false suspicions occurred only once. In control examinations it was not possible to show a certain recurrence in anyone. False suspicions of recurrence were raised for 37 patients (9.3%) in the double-reading arm and 21 (5.6%) in the single-reading arm. In the double-reading arm false suspicions by a clinician amounted to 50.0%, by a radiologist 46.4% and by some other doctor 3.6%. In the single-reading arm false suspicions of recurrence by a clinician amounted to 55.0%, by a radiologist 35.0% and by some other doctor 10.0%. Of all false suspicions of recurrence 12 (20.7%) concerned lung cancer patients, 25 (43.1%) concerned breast cancer patients and 6 (10.3%) concerned lymphoma patients. In the first year of follow-up a total of 23 false suspicions (39.7%) were raised, 17 of them in the double-reading arm. The false suspicions of recurrence in the first year of follow-up appeared to have been caused by radiation therapy changes in the chest radiographies in 86.9%. In the fifth year of follow-up there was no false suspicion of recurrence in either arm. The diagnosis of recurrence was delayed in one patient in the double-reading arm and in 4 in the single-reading arm as no change could be suspected in earlier plain radiographies.

The median period of time elapsing before recurrence of cancer in those with cancer was 1 year 4 months and 4 days in the double-reading arm (range 4 months and 18 days – 4 years, 10 months and 29 days) and 1 year 3 months and 29 days (range 6 months 7 days – 4 years and 2 days), with no statistically significant differences (p= 0.98). The statement of the radiologist did not appear to expedite the diagnosis of recurrence. There was no statistically significant difference (p=0.70) between the arms in the cumulative probability of recurrence (Figure 18).
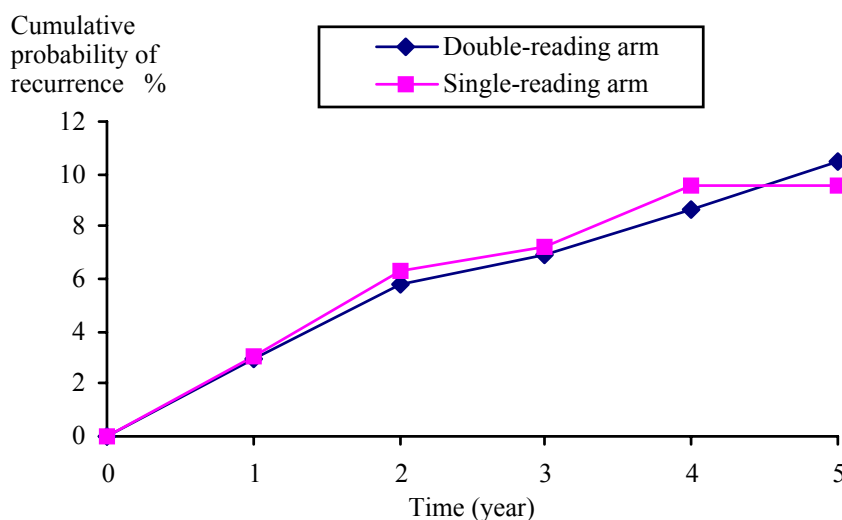

Figure 18. Cumulative probability (%) of recurrence of cancer in plain radiography among patients at the TAUH Department of Oncology in 1991–1997 by year of follow-up and research arm.

Of all recurrences 58.2% (55.6% / 60.7%) were found on the basis of the patients' symptom. Plain radiographies made in connection on routine examinations revealed 36.4% (40.7% / 32.2%) of recurrences. The referral to the examinations included information on the patient's symptoms in 76.9% in the double-reading arm and 71.4% in the single-reading arm. The status finding of the clinician did not lead to a radiograph finding in a single patient. There was 1 recurrence found by chance in connection with another illness in the double-reading arm and 2 recurrences and a new cancer in the signle-reading arm. In the double-reading arm plain radiography served to detect one recurrence per 15 patients, per 134 outpatient visits, per 82 plain radiographies and in the single-reading arm one recurrence per 14 patients, per 122 outpatient visits, per 77 radiographies (Table 13).

In the single-reading arm a recurrence of cancer was found by radiograph in 28 patients, of which a separate request had been made for a radiologist's statement to confirm a recurrence in 21 cases (75.0%), 66.7% of requests were made by doctors in training and 33.3% by specialists.

Local residives were observed in the radiographies for 15 patients from the data as a whole, which was 27.3% of all recurrences. Local residives were observed in radiographies for 25.9% of patients in the double-reading arm and 28.6% in the single-reading arm of all recurrences of cancer detected through radiographies. In both arms these were in patients with lung cancer and lymphoma except for one patient in the single-reading arm who suffered from cancer of the oesophagus.

Metastases were observed in 40 patients. A metastasis as a recurrence finding was observed in 74.1% of those patients in the double-reading arm and 71.4% of patients in the single-reading arm. Of all the metastases 30 were in breast cancer patients, in the double-reading arm these accounted for 43.3% and in the single-reading arm for 56.7%.

Table 13. Number (n) of recurrences of cancer and their cumulative percentual distribution (%) of all recurrences in plain radiography of patients at the TAUH Department of Oncology in 1991–1997 by year of follow up and research arm.

Year of follow-up	Double-reading arm					Single-reading arm				
	n	Cum. %	Total patients	Visits	Plain radiographies	n	Cum. %	Total patients	Visits	Plain radiographies
1	11	40.7	398	1422	888	11	39.3	378	1296	794
2	9	74.1	338	989	566	10	75.0	320	912	545
3	3	85.2	295	702	406	3	85.7	279	672	442
4	3	96.3	235	374	247	4	100.0	222	384	260
5	1	100.0	100	143	100	0	100.0	113	161	103
Total	27			3630	2207	28			3425	2144

Skeleton metastases were found 61.5% of all breast cancer metastases detected in plain radiographies in the double-reading arm and 53.0% in the single-reading arm. A new cancer was detected in one patient in the single-reading arm who suffered from cancer of the thyroid. Radiograph revealed carcinoma of the lung, but it was confirmed as a sarcoma.

In no case was it possible to determine the exact size of the tumour from the radiograph in residive recurrences of cancer detected by radiograph. The average size of tumours measured from metastatic recurrences in the double-reading arm was 3.9 cm and in the single-reading arm 3.5 cm. The size of the metastasis remained unknown in 70.0% of metastatic recurrence findings in the double-reading arm and in 65.0% in the single-reading arm. No difference was found between the arms regarding the average number of known metastases per patient.

5.4.2 Treatment and time of initiation

Treatment for the recurrence of cancer detected in plain radiography was initiated for 77.8% of patients in the double-reading arm. In the single-reading arm a total of 89.3% of patients were treated. A curative treatment target was set for 40.7% in the double-reading arm and 41.4% in the single-reading arm. The median time elapsing between the detection of recurrence and initiation of treatment in the double-reading arm was 8 days (range 0 days – 6 months and 15 days) and in the single-reading arm 6 days (range 0 days – 1 months 20 days). No statistically significant difference between the arms in the time of treatment initiation (p=0.078) was noted. The treatment for recurrence was surgical, radiation or drug treatment or various combinations of these. Treatment with drugs was the most common single form of treatment in both research arms. The most common combination of treatments was radiation plus drug treatment in both arms (Table 14).

Table 14. Number (n) of patients and percentual distribution (%) of all recurrences in plain radiography of patients at the TAUH Department of Oncology in 1991–1997 by treatment provided, year of follow-up and research arm.

Treatment	Double-reading arm		Single-reading arm	
	n	%	n	%
Surgery	1	3.7	1	3.6
Surgery and radiotherapy and/or drugs	1	3.7	2	7.1
Radiotherapy and/or drugs	19	70.4	22	78.6
No treatment	6	22.2	3	10.7
Total	27	100. 0	28	100. 0

5.4.3 Other findings in plain radiography

The radiographies showed 78 other findings in the double-reading arm and 61 other findings in the single-reading arm. In both arms the most common other findings were reaction of the lungs to radiation treatment. In the double-reading arm 28.6% of radiation reactions detected were treated and in the single-reading arm 46.7%. In the double-reading arm inflammation reactions due to reasons other than radiation treatment were found in 10 patients and in the single-reading arm in 8 patients. Treatment was initiated in the double-reading arm in 87.5% of impaired function of the heart found in radiographies and in 50.0% in the single-reading arm. A radiologist's statement had been requested separately on 68.9% of those radiographies in which there was a finding other than recurrence of cancer in the single-reading arm.

5.4.4 Recurrences and new cancers in special radiological examinations

In the data as a whole recurrences of cancer were found through special radiological examinations in 37 patients, which was 16.3% of all recurrences of cancer, 22 (19.3%) in the double-reading arm and 15 (13.3%) in the single-reading arm (Table 15). In the double-reading arm 54.5% of these recurrences were local recurrences and in the single-reading arm 53.3%, with 45.5% metastases in the double-reading arm and 46.7% in the single-reading arm.

Of all recurrences detected by special radiological examinations 24 (64.9%) were found by ultrasound examination, in the double-reading arm there were 17 (77.3%) and in the single-reading arm 7 (46.7%). In both arms mammography revealed 8 recurrences, and 3 were new tumours in the contralateral breast. In both arms one new cancer in the contralateral breast was found through ultrasound examination. CT revealed 1 recurrence in the double-reading arm and 3 recurrences in the single-reading arm. One recurrence in the single-reading arm was found using contrast medium in the oesophagus.

Table 15. Number (n) of recurrences in by special radiological examinations and their cumulative percentual distribution (%) of all recurrences of patients at the TAUH Department of Oncology in 1991–1997 by year of follow-up and research arm.

Year of follow-up	Double-reading arm			Single-reading arm		
	n	cum. %	Total	n	cum. %	Total
1	6	27.3	337	6	40.0	385
2	4	45.5	332	4	66.7	314
3	5	68.2	242	1	73.3	206
4	7	100.0	157	3	93.3	159
5	0	100.0	69	1	100.0	84
Total	22		1137	15		1148

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5.4.5 Recurrences and new cancers by other means

Recurrences of cancer were detected by other means than radiological examination in 135 patients (59.5%) of all recurrences, with 65 patients in the double-reading arm (57.0%) and 70 in the single-reading arm (61.9%). In both research arms more recurrences of the disease were detected in the first year, compared to other follow-up years, 44.6% in the double-reading arm and 42.9% in the single reading arm (Table 16).

Physical examination served to find a total of 98 recurrences, which was 43.2% of all recurrences and 72.6% of recurrences found by other means than radiological examination. Physical examination served to detect 50 (76.9%) recurrences of all recurrences detected by other means than radiological examination in patients in the double-reading arm and 48 recurrences in patients in the single-reading arm (68.6%). Isotope examination revealed 11.0% of recurrences of cancer in the double-reading arm and 14.3% in the single-reading arm of all recurrences detected by other means than radiological examinations. In the double-reading arm 6 new cancers were found and in the single-reading arm 4.

Table 16. Number (n) of recurrences of cancer detected by other means than plain radiography and cumulative percentual distribution (%) of all recurrences of patients at the TAUH Department of Oncology in 1991–1997 by year of follow-up and research arm.

Year of follow-up	Double-reading arm			Single-reading arm		
	(n = 65)	Cum. %	Total	(n = 70)	Cum. %	Total
1	29	44.6	398	30	42.9	378
2	16	69.2	338	15	64.3	320
3	12	87.7	295	8	75.7	279
4	6	97.0	235	11	91.4	222
5	2	100.0	100	6	100.0	113

5.5 Patient's performance status during follow-up

The performance status of patients in follow-up and in non-recurrent phase of cancer on the last follow-up day of the first year was estimated to be good (Zubrod 0) for 469 patients (71.3%) in the data as a whole, for 69.2% of patients belonging to the double-reading arm and for 73.4% of patients in the single-reading arm. Since performance status was assessed on the last visit of each follow-up year, no definition of performance status for the last follow-up year could be made for those patients in whom

the disease recurred. Throughout the period of follow-up there were percentually more patients whose performance status was estimated to be good in the single-reading arm than in the double-reading arm. The difference was highest at the end of third and fourth year (Table 17).

Table 17. Number (n) of patients with good performance status (Zubrod 0) and percentual distribution (%) of all patients at the TAUH Department of Oncology in 1991–1997 by year of follow-up and research arm.

| Follow-up year | Double-reading arm | | Single-reading arm | | Difference |
	n	%	n	%	of percentage
0	279	61.7	285	68.4	−6.7
1	234	69.2	235	73.4	−4.2
2	201	68.1	200	71.7	−3.6
3	159	67.7	167	75.2	−7.5
4	67	67.0	86	76.1	−9.1
5	66	66.0	80	70.8	−4.8

5.6 Recurrent phase of cancer

Those patients in whom cancer recurred or in whom a new cancer appeared at some point during follow-up or whose disease remained metastatic throughout follow-up amounted to 178 (39.4%) in the double-reading arm and 161 (38.6%) in the single-reading arm. The follow-up events after the date of confirmation of recurrence were added to those follow-up events which with regard to their disease belonged with cases remaining metastatic. The total number of visits to the outpatient clinic was 1866, of which 22.7% were in the double-reading arm and 19.0% in the single-reading arm of all the outpatient visits. In the recurrent phase there were 4.2 visits per year of follow-up and no differences between the arms were found. The number of outpatient visits per patient year was greatest in the first year in both arms (5.9/5.4) (Figure 19).

Of all visits the number of extra visits in the double-reading arm was 40.8% and in the single-reading arm 42.3%. There were 1.7 visits in the double-reading arm and 1.8 visits in the single-reading arm per year of follow-up due to doctor's request, the patient's decision or other reasons. Events connected to beginning and ending of care of recurrence of cancer were the most common reason for extra visits in both arms (27.9%/29.2%). The number of extra visits is emphasised in the recurrent phase of cancer compared to the non-recurrent phase, in which the number of extra visits was 11.5%. Of all follow-up visits 63.0% were to specialists, with no difference found between the arms.
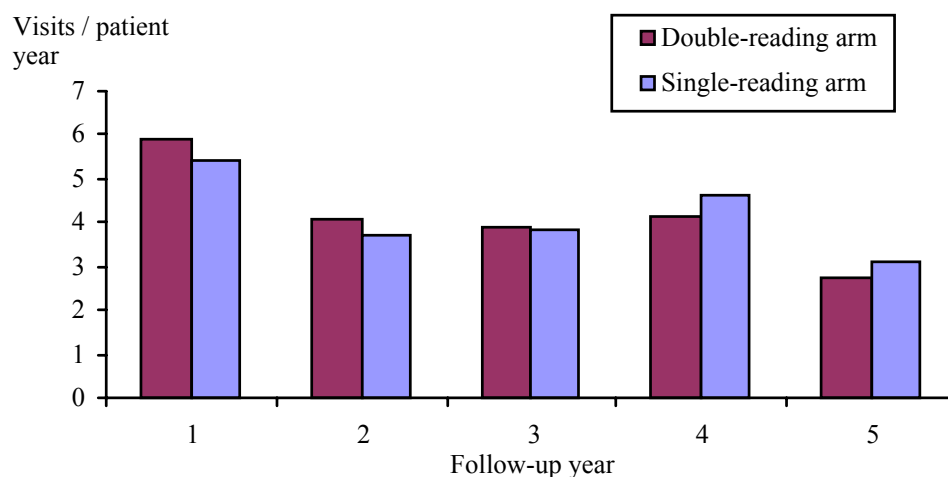
Figure 19. Visits by patients with relapsed disease per patient year at the TAUH Department of Oncology in 1991–1997 by year of follow-up and research arm.

A total of 3020 radiological examinations were made, 32.5% of all in the double-reading arm and 30.0% in the single-reading arm. Of all examinations made 72.0% were plain radiographies and no difference was found between the arms (71.1%/72.8%). In the non-recurrent phase of cancer the proportion of plain radiographies of all radiological examinations was 65.6%. The most commonly made radiography was of the chest, in the double-reading arm 69.5% and in the single-reading arm 70.1%. The proportion of chest radiographies of all plain radiographies in the non-recurrent phase was 85.2%. The proportion of bone radiographies doubled in the recurrent phase compared to the non-recurrent phase. In all follow-up years a radiologist's statement was requested separately for 60.1% of radiographies in the single-reading arm. Quantitatively most statements were requested on chest radiographies. Of bone radiographies most statements were requested of the spine and the ribs, 90.6% of each. The need for statements increased 15.7% in the recurrent phase of cancer compared to the non-recurrent phase. After mammography the most common special radiological examination in both arms was other ultrasound than of the breast (60.5%/55.1%). In the non-recurrent phase the proportion of other ultrasound was 33.5%/33.7%.

5.7 Survival and death

Altogether 19 deaths from cancer were recorded among patients in the follow-up phase, 10 of them in the double-reading arm. Deaths due to other causes in the double-reading arm totalled 12 and in the single-reading arm 7 (Table 18).

Table 18. Number (n) of surviving patients and number (n) of dead patients at the TAUH Department of Oncology in 1991–1997 by year of follow-up and research arm.

Year of follow-up	Double-reading arm			Single-reading arm		
	Alive	Died from cancer	Died from other reason	Alive	Died from cancer	Died from other reason
	n	n	n	n	n	n
1	398	3	2	378	6	1
2	338	2	3	320	2	3
3	295	2	2	279	1	1
4	235	3	4	222	0	1
5	100	0	1	113	0	1
Total		10	12		9	7

A radiologist's statement did not appear to have any effect on patient's survival or death from cancer. There was no statistically significant difference ($p = 0.80$) between the arms in this respect (Figure 20, note scaling).
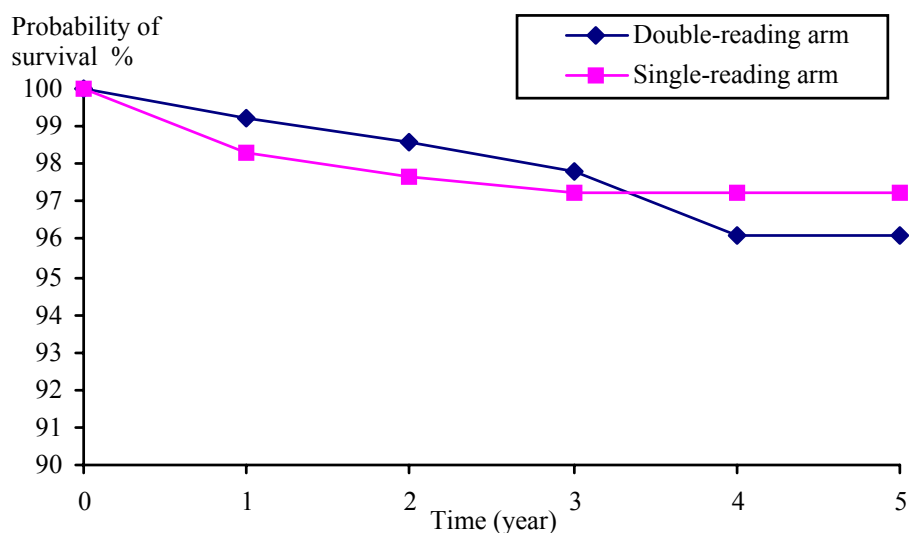

Figure 20. Cumulative survival probabilities (%) of patients classified with non-recurrent disease at the TAUH Department of Oncology in 1991–1997 by year of follow-up and research arm.

In the group with metastatic cancer 77 (82.8%) patients died from cancer and 2 (2.2%) from other causes. Patients transferring to treatment elsewhere amounted to 15.0%. Of all metastatic patients 57.0% died in the first year of follow-up, 53.7% in the double-reading arm and 61.5% in the single-reading arm. Of patients in whom recurrence or new cancer appeared, 129 (52.4%) died from cancer, 49.9% in the double-reading arm and 54.8% in the single-reading arm. Death from other causes was recorded for 5.5% of patients with a recurrence in the double-reading arm and for 3.2% in the single-reading arm. In both arms the cause of death for two patients remained unknown.

Of all patients in the data (869) no difference was found in survival between the two randomised arms during the follow-up (p=0.34) (Figure 21).
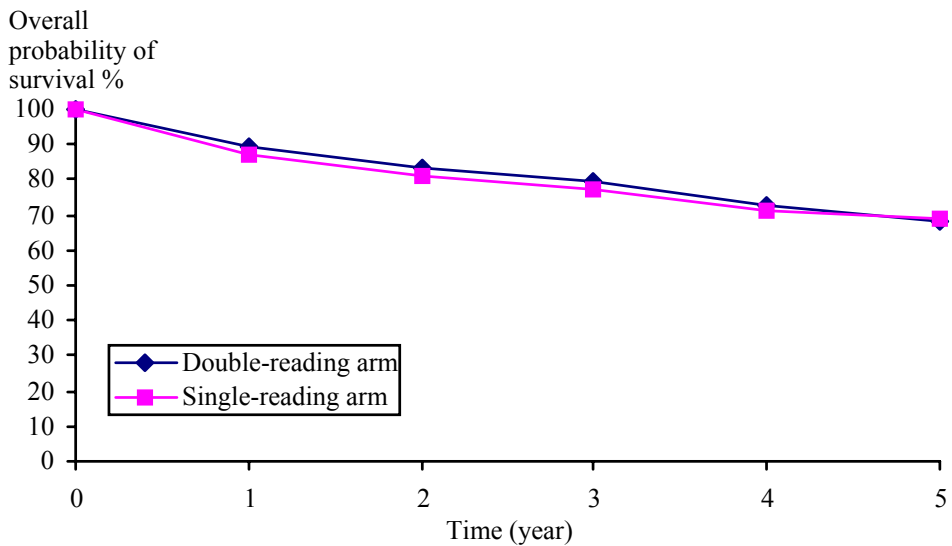

Figure 21. Cumulative cancer specific survival probability (%) of patients at the TAUH Department of Oncology in 1991–1997 by year of follow-up and research arm.

6 Discussion

The radiological follow-up of cancer patients forms part of the overall follow-up after primary treatment, its first objective being to detect possible recurrence of cancer as early as possible, to detect any new cancer and to identify possible negative effects of treatment and to prolong the patient's life. The follow-up of different types of cancer varies according to the characteristics of the disease and the individual. Follow-up for almost all patients lasts virtually for life, although the nature of follow-up changes gradually to resemble a health check-up.

Follow-up by radiology subsumes radiographies of the lungs and skeleton and the statements made on them. There are ample findings in the literature according to which the significance of routine plain radiographies follow-up has been questioned (Ciatto and Herd-Smith 1983, Chaudary et al. 1983, Hietanen 1986, Holli 1987, Ciatto et al. 1989, Rutgers et al. 1989, Løgager et al. 1990, Moskovic et al. 1992, Rosselli Del Turco et al. 1994, GIVIO Investigators 1994, Joseph et al. 1998, Coppola et al. 1999). Follow-up radiological examinations of cancer patients should be done at times determined rather by the natural course of the disease or the patient's clinical condition than according to any rigid programme (WHO 1983).

Numbers of radiographies made have already diminished due to earlier research findings and changes in public opinion in a more critical direction. More radiographies are made on the basis of the individual patient's condition. Prospective studies on the significance of radiological examinations or effectiveness of interpretations of plain radiographies, however, are lacking.

In the present study the significance of the radiologist as the interpreter of plain radiographies in the cancer patient's follow-up has been explored. Significance has been evaluated on the bases of the findings of the radiologist, the consequent additional radiological examinations, extra visits, treatments, the patient's well-being, survival and separately requested statements. For the purposes of the present study an experimental research setting was created with patients (869) in follow-up at the TAUH Department of Oncology during the period 1991–1997.

Procedures for interpreting cancer patients' plain radiographies vary in Finland. The established procedure at TAUH is based on the separate appraisals of a clinician and a radiologist. It is the effectiveness and efficacy of this double reading which is the subject of the present study. The findings with regard to the single reading of the clinician and the double reading by a clinician and a radiologist separately in this study may in part also be applicable to other treatment units in the reorganisation of local radiological work.

The significance and effectiveness of different interpreters of radiographies in clinical practice is most reliably ascertained through random clinical tests, when the systematic number of sources of error diminishes compared to non-randomised examination. A randomised, controlled test is considered scientifically more valid than various empirical research objectives in the evaluation and comparison of the benefits and shortcomings of various medical methods in the examination and care of patients.

The present research setting, the diagnostic test, maximised the comparability of double and single reading. In normal clinical practice the contribution of the radiologist is determined among other things by the type of hospital and thus by the domicile of the patient, the anatomical location of the cancer, its malignity and degree of dissemination, the age of the patient and his or her state of health. Such factors are also prognostic factors of the disease, which may reflect selection and selectivity in addition to the radiologist's influence in non-experimental research. To the best of my knowledge the influence of the radiologist has not previously been researched by means of experimental setting.

The randomisation was accomplished by dividing the cancer patients (869) into two arms as they transferred from primary treatment to follow-up. The plain radiographies of the first arm were examined by both a clinician and a radiologist separately (double reading), while those of the patients in the second arm were examined by a clinician only (single reading), and separately at the discretion of the clinician, by a radiologist at separate request. The experimental arrangement concerned only the procedure for interpreting plain radiographies at the Department of Oncology.

Although the practical arrangements for the study were explained in writing and verbally before the beginning of the research, it proved difficult in the hectic pace of clinic work to remember the definition of the patients' randomisation for the study and the time of the randomisation. Regular reminders to the personnel of the Department of Oncology about the research proved essential. Of all the randomised patients 22% were excluded from the study and the most common reason was incorrectly defined randomisation time (11%). No difference was noted between the research arms with regard to errors occurring in randomisation. No intentional or unintentional selection of patients into either of the arms or into those excluded from the study was disclosed either at the frequent supervision visits or otherwise in the field work. The smaller size of the single-reading arm (417/452) compared to the double reading arm is largely explained by the difference of odd and even-numbered days. Randomisation divided the patients within the bounds of chance into arms of the same size. A statistically significant difference emerged in the age distribution of women in the two randomised arms. On the other hand the median difference in the ages of the women was only one year (57/56 years). The proportion of younger women was emphasised in the single-

reading arm. If there had been intentional selection based on age, it might have been assumed that the proportion of younger women would have been greater in the double-reading arm, when younger patients would have been offered optimally comprehensive radiograph follow-up. There was a statistically significant difference between the arms in the overall number of local cancers, but in the number of local cancers by organ no difference was noted between the arms. No statistically significant differences emerged regarding sex, the age of men, confirmation of cancer diagnosis, size of tumour, cancer type, primary cancer treatment and response to this and the performance status of the patient after primary treatment.

In the present study breast cancer patients accounted for 59% of all patients. The proportion of breast cancer patients for the same period of time was 15% (Finnish Cancer Registry 1993, 1996, 1997, 2000). Such a great difference is due to the fact that of the patients receiving primary treatment at the TAUH Department of Oncology, the majority are breast cancer patients and a considerable part of them remain for follow-up. In this study different cancers appear numerically in a very different way and it is the arm of breast cancer patients and their number (516) which may be considered sufficient to permit conclusions to be drawn. In earlier studies, most of which have been non-experimental and retrospective, patient numbers have varied greatly. Only two prospective randomised studies could be found in the literature on the importance of radiographies in the follow-up of breast cancer patients (Rosselli Del Turco et al. 1994, GIVIO Investigators 1994). However, none of these addresses the importance of the radiologist. The data in the study by Rosselli del Turco et al. (1994) comprised 1243 patients divided among 12 separate research centres. The report published by the GIVIO researchers (1994) addressed a patient population of 1320 patients divided among multi-centre research at 26 different hospitals. The present study is the largest one to be carried out at a single hospital, and in general one of the few from which selectivity in giving statements has been eliminated by randomisation.

Hietanen (1986) found 19% of all recurrences of breast cancers by chest radiograph and Ojeda et al. (1987) 9%. In this study 12% of all recurrences of breast cancer were detected by chest radiograph. The discrepancies are due to variation in follow-up duration and in patient selection between the studies. According to the literature, recurrences have been found in less than 0.4% of all chest radiographies made of breast cancer patients (Vestergaard et al. 1989, Moskovic et al. 1992). In this study 1% recurrences of cancer were found through chest radiographies. According to the literature a considerable proportion of cancer patients' recurrences has been detected through physical examination and history information (Schapira and Urban 1991, Schapira 1993, Rosselli Del Turco et al. 1994). The findings of this study show that through clinical examination alone 39% of recurrences of disease were detected. These

results support the importance of physical examination in breast cancer follow-up and reveal the slight significance of radiographies in the detection of recurrence of cancer.

In present study 75% of the recurrences of cancer detected through plain radiographies were found within the two first years of follow-up. The figure depends on duration of follow-up and thus the different readers of the examinations cannot be compared to each other. In this study the mean duration of follow-up was 3.3 years, which may be considered reasonable. While the study was being conducted, only three patients (2/1) after follow-up returned to the Department of Oncology for treatment of a recurrence. None of these patients' recurrences was detected through radiography. In this study the number of recurrences detected by plain radiography was greater in the single-reading arm than in the double-reading arm. This could be mere coincidence. On the other hand the clinician knows more than the radiologist about the patient's symptoms and disease when he or she examines the plain radiographies. It may be assumed that the study itself caused the plain radiographies to be read with greater meticulousness in both arms. Radiologists interpreting the radiographies totalled 20 and clinicians 27. The number of doctors reading the radiographies may be considered reasonable for general deductions and questions of individual professional skill are not necessarily emphasised.

The number of recurrences found by plain radiographies among lung cancer patients in the double-reading arm was 2.5 times that in the single-reading arm. A parallel difference can also be seen between the arms for number of false positive findings. The radiologists began to suspect recurrence of cancer early in follow-up although the findings in the plain radiographies could frequently be explained by reactions to radiation therapy. This was also partly caused by insufficient information on the referral regarding the patient's symptoms and other possible examinations. Because changes due to radiation treatment rendered interpretation of the plain radiographies more difficult, 30% of lung patients were falsely suspected of having a recurrence of cancer. Bourguin et al. (1987) propose a corresponding figure of 29%. Perception of radiation treatment changes in chest radiography is not sufficient cause to commence treatment of a patient without symptoms, as became very clear in this study. Generally the doctor giving the treatment estimated, whether there is a connection between radiological findings and the patient's clinical condition or not.

The difficulty of interpreting radiograph findings is evidenced by the fact that in not one local recurrence was it possible to determine the exact size of the tumour. This was mostly due to the radiation changes to be seen both for patients with lung cancer and for patients with lymphoma. In the double-reading arm treatment, mostly steroid treatment of the patient was initiated in 29% of radiation reactions found in radiographies, the corresponding figure for the single-reading arm being 47%. It must

be assumed that on detecting a radiation reaction in the radiograph the clinician ascertains the patient's symptoms and if necessary initiates treatment on the basis of the symptoms alone. In the double-reading arm the clinician saw the radiologist's statement afterwards and if the patient had no symptoms, no treatment was initiated.

As a whole 42% of the patients for whom a recurrence of cancer was found in plain radiography had no symptoms. The median time elapsing between the detection of the disease to its recurrence was 5 days shorter in the single reading arm than in the double reading arm. The radiologist's statements did not accelerate the recurrence diagnosis. Treatment for recurrences of cancer found in radiographies was initiated more frequently in the single-reading arm than in the double reading arm. This can partly be explained by the fact that, among the recurrences of cancer in the double-reading arm, there were more lung cancer patients than in the single reading arm (37% / 14%), for whom at the point of recurrence there is not necessarily any beneficial treatment available or because of the general condition of the patient no treatment could be given. There were no differences between the arms regarding median time elapsing between detection of all recurrences and initiation of treatment.

The performance status measured by Zubrod scale was somewhat better in the single-reading arm, the proportion of score 0 was 68% and in the double-reading arm 62% respectively in the beginning of the follow-up. There was some variation in the prevalence of score 0, but the difference persisted in average throughout the follow-up period. The difference may be related to the different age distribution in the two arms. Age distribution can also partly explain the fact that the difference is highest at third and fourth years.

Information on the patients' performance status was well documented in the medical histories, but in this study information on the patients' performance status was gathered only on the basis of the last follow-up visit of each follow-up year. Thus variations in performance status in the course of the follow-up year do not emerge at all. This study does not give any obvious indication that double-reading had any effect on the patient's performance status. It is also difficult to estimate and measure the direct effect of the radiologist's statements on the patient's physical well-being.

It would appear on the basis of the study that the radiologist's statements on the plain radiographies had no effect on the patient's survival or death from cancer. No differences in survival were found between the randomised arms.

Paakkala (1982) noted that doctors in health centres requested a radiologist's statement on 50% of all radiographies, there was no difference found between permanent health centre doctors in the number of consultations requested. A radiologist's statement was requested on an average 10–25% of all plain radiographies done in health centres (Kinnunen et al. 1997). Variation occurred in the catchment area

and the number of radiologist's statements requested was influenced by the availability of statements and their prompt delivery. In this study approximately the same number of radiological examinations were done in each of the randomised arms, which is a further reason for the success of the randomisation and the comparability of the arms. Thus randomised arms can be compared and a direct assessment can be made of the significance of the radiologist's contribution. Separately requested radiologist's statements accounted for 44% of the radiographies in the single-reading arm. In the study by Paakkala (1982) health centre doctors frequently requested statements on spine radiographies. In this study, too, more statements were requested on spine radiographies compared to others. The clinician wished to confirm his or her own interpretation by requesting a radiologist's statement to be sure. Doctors in training requested a radiologist's statement on plain radiographies somewhat more frequently than specialists. Frequently there was no urgency to receive the statement as such, which serves to explain the small number of occasions on which the clinician visited the radiologist for purposes of consultation. The need to request radiologists' statements grew after recurrence of cancer. In all the follow-up years radiologists' statements were separately requested for 60% of the total number of plain radiographies in the recurrent phase. However, the situation is very different compared to the non-recurrent phase. The patient may have symptoms and in any case a dissemination of cancer for which there is a greater need to ascertain the response to treatment and the negative effects through the radiologist's assessment than to assess plain radiographies of the non-recurrent disease.

It has been proposed that radiographies and other examinations be concentrated on detecting metastases in patients with symptoms (Winchester et al. 1979, Wickerham et al. 1984, Joseph et al. 1998). These examinations can usually be done in the health care unit of the patient's place of residence. On the basis of the symptoms and the results of tests the patient's referral to the Department of Oncology or to the unit at which the primary treatment was provided can be considered.

Earlier studies emphasise the importance of information on the patients' symptoms in the interpretation of plain radiographies (Tudor et al. 1997), for breast cancer patients it is more important to detect bone metastases (Tereso-Tess et al. 1981, Valagussa et al. 1982). In this study the information on the patients' symptoms was well conveyed in the referrals in the double-reading arm (76.9%), thus further information on symptoms would hardly have affected the final results. In the present study no differences in survival or performance status were found between patients in the double-reading and single-reading arms in the non-recurrent phase. There were clear differences in costs between the arms. The saving in radiologist resources was 56% for single-reading, which is considerable. Double-reading has been found to be applicable

for mammography screening, sensitivity having been found to improve 10%–14% (Anderson et al. 1994, Warren and Duffy 1995). However, it is a totally different matter to seek to detect an early cancer which is entirely curable than to seek a recurrence of the disease to little avail with excessive resources. There is justification for seeking recurrences without symptoms if the disease can be cured with treatment even after it has recurred. On the other hand detecting recurrences cannot be justified only by the patient's symptoms. In a questionnaire administered to breast cancer patients by Jäger et al. (1996) a remarkable number of patients had symptoms. However, the number of patients with symptoms did not correlate with the metastases detected. One may speculate that symptoms arising from early metastases are confused with other symptoms and are thus not sufficiently specific in clinical examination.

On the basis of this study it may be concluded that if necessary, a considered request for a statement may be made and the capacity of specialists enlisted in work if its benefit can be proven. The capacity of radiologists released from routine dictation could be harnessed by increasing the meetings between radiologists and oncologists at which problem situations arising could be tackled and at which doctors with less experience would have an opportunity to learn.

The structural reform of the division of labour in the treatment and follow-up of cancer between primary health care and specialist nursing is under way. More tasks will be allotted to the health centres for the overall management of cancer (STAKES 1993) and cancer patients will be followed up more in the health centres. However, the health centres do not necessarily have the functional capability to take on a greater proportion of the responsibility for management of cancer than they have at present, as has been shown by a questionnaire survey administered to health centre doctors in Pirkanmaa Hospital District in 1997. The survey indicated a perceived need for further training in cancer follow-up among other things (Kosunen and Lammi 1998). A considerable proportion of radiographies for cancer follow-up will also be transferred to the health centres, either the health centre of the patient's place of residence or according to the system of centralisation to a health centre in an adjacent municipality. In any case health centre doctors will be assessing more plain radiographies of cancer patients than before. According to a study published by Kinnunen et al. (1997) the success rate of health centre doctors in interpreting radiographies was 68%. Teaching of plain radiography interpretation to health centre doctors could be intensified, for example, by teleradiology, when health centre doctors would have the option of consulting with a radiologist directly and without delay. However, the finding in this study of the slight significance of double reading in the follow-up of cancer makes it not directly applicable at health centre level. The abilities of specialists in cancer treatment in the hospitals are totally different from those of health centre doctors. Radiologist capacity

released from routine dictation of plain radiographies could be used to make specialist care internally more effective by investing more than before in the primary diagnosis of cancer, in special examinations in follow-up and in teaching activities. Moreover, it is necessary to safeguard the level of radiological diagnostics at the level of primary health care through continuing education, for which applications of new technology provide better opportunities than before.

In this study the effect of radiologist was assessed on the numbers and types of visits, doctors in the outpatient clinic, numbers and types of radiological examinations, doctors at the Department of Radiology, need for a statement by a radiologist and recurrences and new cancers found by radiological and other methods. The present study shows that the benefit to the patient of double-reading of plain radiography is slight. In the double-reading arm no more recurrences of cancer were found, nor were they found any earlier, nor was treatment begun any sooner than in the single-reading arm. From the patient's perspective it may do more harm than good that possibly meaningless changes are found when plain radiographies are assessed in retrospect, causing patients further tests and visits to the outpatient unit and thus possibly impairing quality of life. The significance of the radiologist for the entire research is more in the nature of consultation for radiographies. From the perspective of the organisation double-reading of radiographies cannot be justified, if lack of resources has been shown. If changes are made in the present procedure of double-reading, then constant training of clinicians in the interpretation of plain radiographies should be ensured, likewise the availability of radiological consultation.

7 Summary

Cancer is becoming increasingly common in Finland, due above all to changes in the age structure of the population, the improved results of cancer treatment and the improved prognosis for cancer due to early diagnosis. The future challenge to health care will be not only the growing number of cases of cancer but also the larger number of those in follow-up. It is important to estimate how our health care system will cope with the treatment of cancer and follow-up maintaining at least the level of performance achieved so far.

The present study investigated the patients' follow-up after primary treatment principally by assessing the significance of plain radiographies and especially the person interpreting them from the perspective of the patient regarding identification of recurrence, treatment of recurrence, physical well-being and survival. An assessment is moreover presented of the significance of the person interpreting the plain radiographies from the perspective of the organisation in resources expended. For the purposes of the research an experimental setting was arranged in which cancer patients in the beginning of follow-up after primary treatment were randomised into two arms, referred to as double-reading and single-reading arms. For patients in the double-reading arm the plain radiographies were interpreted first by a clinician and then by a radiologist, each separately. For patients in the single-reading arm the plain radiographies were interpreted by a clinician alone, but if necessary a radiologist's statement could be obtained by separate request. The research is prospective and based on retrospectively collected medical histories. The data consists of cancer patients transferring to follow-up at the TAUH Department of Oncology during the period 1991–1997. The total number of patients was 869, with 452 in the double-reading arm and 417 in the single-reading arm. The patients continued to participate in the research until follow-up ended in death, removal, change in level of follow-up or other reason or by 31.12.1997. The patients' diagnoses, dissemination of the disease and primary treatment provided were analysed. Data were collected on the patients' follow-up from each visit made to the Department of Oncology and from all radiological examinations made in TAUH. The information so obtained was analysed by year of follow-up and between the two randomised arms. Recurrences of the disease detected by plain radiography and other methods and new cancers occurring during the follow-up period were also analysed. The significance of the radiologist, both in the non-recurrent and recurrent phase of cancer was assessed.

Randomisation divided the patients within the bounds of chance into two comparable arms of equal size. The number of women and thus of breast cancer in the

data is emphasised compared to other cancers. This is due to the fact that the majority of patients entering follow-up at the TAUH Department of Oncology are suffering from breast cancer. The median duration of follow-up in both research arms was over three years. The length of follow-up was influenced primarily by the follow-up procedure of university hospitals. Follow-up conducted at TAUH varies depending on the cancer and its nature. On the one hand during the period of the study only three patients returned to follow-up for treatment of disease which had disseminated after the end of follow-up. With respect to follow-up visits and radiological examinations, the research arms were very similar during the first three years of follow-up, differences appeared to emerge to some extent in the fourth and fifth years, but the differences were due to other reasons than plain radiography procedures.

In the data as a whole recurrences of cancer were found in about 29% of patients of both arms. Almost equal numbers of completely new cancers were found in both randomised research arms. Recurrence of cancer during the study appeared to concentrate on the first three years of follow-up and the cumulative effect over the first four years was very similar in both research arms. Recurrence of cancer was found by plain radiography in 7% of patients, accounting for 24% of all recurrences. Less than one third of all recurrences identified through plain radiography were local recurrences, the remainder being metastases. Double-reading did not appear to improve early detection of recurrence, nor did double-reading reveal more recurrences of the disease compared to single-reading. In more than one half of cases recurrence of cancer was found by plain radiography on the basis of the patient's reported symptoms. Double-reading did not appear to accelerate initiation of treatment of recurrence, nor to improve the patient's performance status or survival. With regard to other findings through plain radiography, double-reading did not appear to offer any clear benefit compared to single-reading. Radiation reactions seen in plain radiography were of importance to treatment only if the patient had symptoms.

The oncologist requested a radiologist's statement on less than one half of all the plain radiographies in the single-reading arm. Generally this was requested for purposes of confirmation, and the need appeared not to be dependent on year of follow-up or primary site of tumour. Differences in numbers of statements requested by different clinicians could be explained by differences in experience and workload. It emerged that interpreting chest radiographies was easier for the clinicians than interpreting bone radiographies. The saving in radiologists' work through single-reading was considerable. The need for radiologist's statements increased, when cancer had disseminated, which can be explained by the more complex situation response to treatment and negative effects compared to the non-recurrent phase of the disease.

On the basis of the present study it can be stated that plain radiography alone seldom results in detection of recurrence of cancer and that double-reading of images does not offer any extra essential benefit for the patient. The significance of the radiologist in the interpretation of plain radiographies is emphasised more in a consultative function. Thus the contribution of the radiologist could be focussed on interpretation of radiological examinations in the primary diagnosis of cancer and in special radiological examination during follow-up.

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