Sakari Mustakallio — Pioneer in cancer research

A Finnish Pioneer in Cancer Education, Medical Radiology and Radiotherapy

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Sakari Mustakallio was born on 9 January 1899 in Kuopio, eastern middle Finland, where his father was a cathedral dean. Mustakallio studied medicine at the University of Helsinki and received his medical degree in 1929 and his PhD in 1934. He presented his doctoral thesis on ostitis fibrosa localisata at the Department of Pathology and began his practical medicine at the Department of Surgery, and then continued in radiology, which at that time was a combined speciality including both x-ray diagnostics and x-ray therapy. He was well prepared for his work as a cancer doctor, having experience in both pathology and surgery in addition to diagnostic radiology and radiotherapy.

In his pioneering activities, Mustakallio concentrated on cancer treatment by combined modalities. A combination of conservative surgery and radiotherapy created the prerequisite for breast-saving treatment. Mustakallio also laid the foundation for intraoperative roentgen therapy, which he used mainly in carcinoma of the urinary bladder, but also in carcinoma of the pancreas and stomach.

The year 1936 was an important one for cancer care in Finland. The Cancer Society was founded that year and in the same year the Radiotherapy Department in Helsinki was established. Mustakallio was at that time head of the x-ray department of the Finnish Red Cross Hospital in Helsinki, where he practised both diagnostics and roentgen therapy. The National Board of Health appointed Mustakallio as head of the Department of Radiotherapy connected to the University of Helsinki as a part of the General Hospital of Helsinki. He accepted the appointment on two conditions, he wanted a pathologist and a physicist in the department. Both conditions were accepted, but the physicist only after some confused discussions (1, 2).

After being appointed as Head of Department, Mustakallio visited the Radiumhemmet in Stockholm and its head, Elis Berven, one of his good friends. The roentgen and radium treatment methods of Radiumhemmet, also including bipolar electrocoagulation, were introduced in Helsinki. Two years later Mustakallio visited several radiotherapy departments in the United States. The newly established department, the Central Institute of Radiotherapy, was equipped with x-ray therapy machines and from 1938 with telecurie apparatus, a teleradium unit with 5 g radium. In addition, the department had an operating theatre for biopsies and minor surgery and a room for intracavitary radium treatment of gynaecological cancer and head and neck cancer, 58 beds, and a pathology laboratory and x-ray diagnostic unit.

Mustakallio's scientific career started with his thesis. He carried out some studies on giant cell tumours of the bone, gastric cancer, oesophageal cancer and lung cancer. On skin cancer and its radiotherapy, he published an extensive study (3). Very soon he developed an increasing interest in breast cancer, and this also became his main scientific field. In later years he adopted hormonal treatment for breast cancer, about which he was very enthusiastic.

In 1945 he published his first paper on the possibilities of roentgen therapy in the treatment of breast cancer (4). He reported the results of 384 patients treated postoperatively during the period 1936–1943.This material included 23 patients who had refused radical surgery. These patients were treated by conservative surgery, lumpectomy, carried out in most cases by Mustakallio himself at the Department of Radiotherapy. He also personally treated the patients postoperatively with x-ray therapy. Only one recurrence was observed during the follow-up period of 1–5 years.

With regard to the good results achieved by the conservative roentgen-surgical treatment in 23 cases of early stage breast cancer, Mustakallio suggested a more conservative treatment instead of radical surgery, which according to him tended to weaken the general resistance to cancer. For early stage breast cancer, Mustakallio recommended preoperative roentgen therapy, simple extirpation of the tumour and subsequent intensive roentgen therapy

of the axilla and clavicular fossa. He was thus one of the early advocates of conservative treatment of breast cancer. In his paper in 1945 he concluded that distant metastases did not spread postoperatively, but during the operation. Radical surgery seemed unnecessary in cases where the primary tumour could be extirpated and where there were no axillary metastases. He considered breast cancer a systemic disease.

In 1954 the material had grown to 127 patients, the 5-year survival rate being 84% (5). Mustakallio now recommended primary extirpation of the tumour followed by histopathological examination. Postoperative roentgen therapy was then given to the supraclavicular region, from both sides to the breast and to the axilla both from the front and the back, 6×3.5 Gy to all fields as skin dose. The axilla was not emptied. Two surgeons, who in the early days acted as Mustakallio's assistants, later continued to perform the resections. It is perhaps worthwhile noting that only two surgeons accepted the method.

In his final report, in1972 (6), Mustakallio analysed a material of 702 patients, 418 of whom had a follow-up of at least 10 years, while 102 patients developed local recurrence or regional metastases. This report was based on his more than 30 years' experience. Some borderline cases of clinical stage II had been included in the material. Mustakallio had no such control material as is required today, but in comparison to historical controls and materials published in the literature, Mustakallio's results were always equally as good as those achieved with radical surgery and postoperative radiotherapy, or more carefully expressed, certainly not poorer. The relative 5-year survival rate was nearly 79% and the 10-year survival rate 75%. These results are similar to those achieved in randomized trials on breast-conserving therapy recently reviewed by Lichter (7). Mustakallio's method did not become more widely accepted in Finland until favourable results from France and the USA were reported. Nobody is a prophet in his own country.

The same policy was continued at the department after Mustakallio's retirement. Rissanen and P. Holsti conducted a retrospective comparison of the results of radical mastectomy and local excision in a material of 866 patients treated between 1948 and 1961 (8). In this material, 527 patients were treated with radical mastectomy and radiotherapy, and 339 with local excision and radiotherapy. In conservative treatment the roentgen dose was 25–30 Gy to the breast in the course of two weeks. The crude 10-year survival rates were as follows: T1 tumours: the radical group (70 patients) 77%, the conservative group (150 patients) 73%, and T2 tumours: radical (457 patients) 64% and conservative (189 patients) 49%. The difference in survival was mainly concentrated to the oldest age group, those over 65 years.

Mustakallio's second main interest in cancer and radiotherapy was head and neck cancers. One interesting paper was the report on the roentgen treatment of carcinoma of the larynx and hypopharynx (9). Among 203 patients with larynx cancer treated during 1936–1943, Mustakallio tried to increase the total dose in 3 patients by treating them twice a day. The normal skin dose was 2.5 Gy per field, total skin dose 60 Gy. In these three patients the treatment was $1.5 \text{ Gy} \times 2$ per day up to 70 Gy total skin dose. The skin reactions were so severe that he did not continue this type of treatment. One of his praiseworthy initiatives was to start a larynx polyclinic. Once a week the residents examined and saw follow-up patients treated for larynx cancer.

Mustakallio also compared the microscopic structure and the radiocurability of laryngeal cancer (10). In addition, he analysed the outcome of radiotherapy in nasal and paranasal carcinomas (11).

A less known of Mustakallio's activities was intraoperative radiotherapy. He planned the new radiotherapy department which opened in 1962. This eight-floor building was a small-scale cancer hospital that included all the necessary activities for cancer treatment and examination, such as radiotherapy, later also chemotherapy, surgery, pathology, a clinical laboratory, x-ray diagnostics, nuclear medicine and 125 beds. It was equipped with a combined surgery and radiotherapy unit in which the operating and radiotherapy rooms were adjacent. The operating table could easily be moved into the radiotherapy room. The x-ray machine was a 250 kV apparatus with ceiling fixture. Mustakallio never had his IORT experiences published in English, only in Finnish with an English summary (12), but a complete manuscript which he presented at the 40th anniversary meeting of the Finnish Radiological Society in 1964 has been preserved (13). The material on bladder cancer was updated later by Appelqvist & Salmo (14). Mustakallio's series included 42 patients with bladder cancer. The single dose ranged from 20 to 40 Gy, average dose being 35 Gy. In 20 patients the direct therapy was completed with external cobalt treatment, maximum dose being 45 Gy and minimum dose 40 Gy. In 21 patients the carcinoma was found to have disappeared completely at cystoscopy. The crude survival and relapse-free survival up to 10 years was analysed according to T stages. The side effects were rather brisk. Complications of different kinds developed in eight patients.

Very early on, Mustakallio realized that the fight against cancer had to be conducted on a broad front. He was very active in writing and giving speeches to people in order to educate and inform them about cancer. He wrote a textbook for nurses on cancerous diseases and their treatment, and conducted lectures for medical students and gave bedside teaching. He was one of the founding members of the Finnish Cancer Society.

Sakari Mustakallio was an active man. He was Dean of the Medical Faculty at the University of Helsinki, President of the Finnish Cancer Society for about 15 years, and

President of the Finnish Radiological Society. During World War II he was the medical head of the Finnish air protection, his military title was that of Lieutenant Colonel. Later, he was appointed chairman of the National Consultative Committee on Radiation Protection, and chairman of the Nordic Committee of Radiation Protection. In recognition of his outstanding work, Mustakallio was bestowed the title Honorary Member of the British Society of Radiology.

Mustakallio was a purposeful person, but also a very kind and helpful senior to his staff, residents and nurses. He was a skilful botanist and had a herbarium that included more than 2 000 plants collected in Finland and in Central European countries. Farming was his way of relaxing; even at the age of over 80 years, he could be seen driving a tractor around his farm.

Sakari Mustakallio was the pioneer, leading figure, and grand old man of radiotherapy in Finland. His activities included conducting scientific work in radiology and radiotherapy, and training the majority of radiologists and radiotherapists in the country between 1936 and 1967. He was appointed Professor of Medical Radiology at the University of Helsinki in 1950, from which post he retired in 1967. Radiodiagnostics and radiotherapy became separate fields in 1964.

Mustakallio died in Helsinki in December 1989, on the brink of his 91st year. Sakari Mustakallio has earned a permanent position in the international radiotherapy community, especially because of his breast-saving treatment method. This symposium has been arranged in honour of his lifework.

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