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REVIEW ARTICLE

Clinical Physiology and Functional Imaging

The birth and development of clinical physiology in Finland

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Scandinavian Society of Clinical Physiology and Nuclear Medicine

Abstract

The specialty of clinical physiology was established in Finland about 20 years later than in Sweden. In the early 1960s, six physicians working mainly in preclinical departments of physiology were certified as specialists in clinical physiology. Many of the first specialists working in hospitals received specialist training in Sweden. The first hospital laboratories of clinical physiology were established in Tampere Central Hospital and Turku University Hospital in 1968. Thereafter, laboratories of clinical physiology were also established in Helsinki University Hospital and in Kuopio University Hospital and later also in most central hospitals. After clinical physiology laboratories were set up in hospitals and the number of specialists increased, the specialty gradually had more impact in clinical work. In the 1999 reform, nuclear medicine, which had previously been a subspecialty, was combined with clinical physiology. Arto Uusitalo was nominated the first professor of clinical physiology in Tampere University in 1984. The first professor in Helsinki University was Anssi Sovijärvi (1994), in Kuopio University Esko Länsimies (1998), and in Turku University Jaakko Hartiala (2003). Today, at four universities professors of clinical physiology and nuclear medicine lead research and medical education in this specialty. The hospital laboratories have modern equipment, which promotes multidisciplinary research with clinicians in fruitful collaboration. The Finnish Society of Clinical Physiology was founded in 1975. Today, it has about 160 members, about half of whom are specialists in the field. On its 40th anniversary, the Society decided to publish the history of clinical physiology in Finland.

KEYWORDS

clinical physiology, Finland, history, nuclear medicine, society, specialty

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1 | DEVELOPMENT OF CLINICAL PHYSIOLOGY AS AN ESTABLISHED MEDICAL SPECIALTY

1.1 | The origin of clinical physiology

Clinical physiology was originated in Sweden during the Second World War. The pioneer was a Swedish doctor Torgny Sjöstrand. He received his degree in medicine in 1935 and was nominated associate professor in pathologic physiology in the next year at the Karolinska Institutet in Stockholm. In this study, the term associate professor is used for the English translation of a docent which has been commonly used in Finland.

The very first laboratory of clinical physiology was created by him in 1942 at the Karolinska Hospital. Clinical physiology became an independent academic medical discipline in 1947 when Sjöstrand was nominated as the first professor of clinical physiology at the Karolinska Institutet. Sjöstrand developed many physiological methods for clinical use, like clinical exercise tests with ECG and blood pressure measurements, the orthostatic tolerance test and several lung function measurements. His principal idea was that in the laboratory of clinical physiology patients from any clinical area could be studied to assess diagnostic changes in body functions and mechanisms for restricted body functions by exploiting the rapidly developing medical technology.

After the Second World War in 1948, Sweden decided to establish professor chairs of clinical physiology to all universities, and clinical physiology became an obligatory part of education for medical students. The Royal National Board of Health decided in 1955 that a central laboratory of clinical physiology must be established in all hospitals in Sweden. These actions promoted rapid development of the discipline in Sweden, both at universities and in hospitals.

Laboratories of clinical physiology were first established in university hospitals: in 1955 in Gothenburg, in 1957 in Umeå, in 1958 in Uppsala, in 1962 in Lund, in 1963 in Malmö and in 1964 in Linköping. In 1989, almost all large hospitals in Sweden had laboratories of clinical physiology, and the number of professor chairs was nine.

In Denmark, the development of clinical physiology was combined with the activities of nuclear medicine. In 1982, the specialty of clinical physiology and nuclear medicine was established. The number of laboratories in that discipline increased rapidly, and in 2019 there were already 15 hospital laboratories of clinical physiology and nuclear medicine in Denmark.

In Norway, clinical physiology was an independent medical specialty in the 1970s, but in the 1980s that branch was combined with cardiology and pulmonary medicine.

1.2 | The specialty is gradually established

The pioneers in the field of clinical physiology in Finland were physiologists working outside hospitals.

The first of them was **Robert Tigerstedt** (1853–1923), who was in 1900 invited back to Finland from a professorship of physiology in the Karolinska Institutet in Stockholm to become a professor of physiology at the University of Helsinki. Before, he had worked together with Carl Ludwig in Leipzig. His main research interest was cardiovascular physiology. He wrote the textbook 'Lehrbuch der Physiologie des Menschen I und II' (1897–1898), which was widely used internationally. Together with P. G. Bergman, he described a blood pressure elevating substance excreted by the kidneys, which was later named renin. He established in the Department of Physiology a laboratory to test the physical and psychological suitability of airplane pilots for flying in 1923.

Kaarlo Hartiala (1919–2009) started his research career also in the Department of Physiology at the University of Helsinki. In 1948–1950, he worked at the University of Chicago, which was made possible by an award from the Rockefeller Foundation. He completed his specialty training in internal medicine before he was nominated 1955 as the first professor of physiology in the University of Turku, the second medical school in Finland. His main research interest was mechanisms of detoxication of xenobiotics in the alimentary tract, where he described the mechanism of glucuronide conjugation. These studies were supported by the United States N.I.H. for over two decades. He established the first cardiorespiratory research unit in Finland in the Department of Physiology to perform cardiac catheterisations and surgery. The first open-heart surgery was performed thereby associate professor Sauli Viikari in 1960. Hartiala also established the Sports Medical Research Unit in Turku and later was the chief physician of the Finnish team in several Olympic Games and one of the earliest fighters against doping in sports.

Martti J. Karvonen (1918–2009) also started his research career in the Department of Physiology at the University of Helsinki. He completed his doctoral dissertation in 1950 at Cambridge University. He was among the first to study the effects of nutrition and physical activity on chronic diseases and worked closely with Ancel Keyes to explore the causes of the postwar epidemic of heart diseases. He has worked as the chief of the Department of Physiology at the Finnish Institute of Occupational Health in Helsinki, then as the chief of the Finnish Institute of Occupational Health and later as the chief physician of the Finnish Military Forces, in addition to serving as the president of the Finnish Medical Association and Finnish Heart Association.

The following physicians became the first specialists in clinical physiology in Finland after being awarded the specialty by the Finnish Medical Board, based on their experience in the field: Kaarlo Hartiala (1960), Eva Hirsjärvi (1961), Tuomas Peltonen (1961), Leo Hirvonen (1962), Martti Karvonen (1964) and Samuli Sarajas (1966). They all had a strong background in physiology. Also, Peltonen and Hirvonen worked in the Cardiorespiratory Research Unit in the Department of Physiology at the University of Turku, and Hirsjärvi and Sarajas in the Department of Physiology at the University of Helsinki.

1.3 | Finnish physicians trained in Sweden

In Finland, clinical physiology as an independent medical discipline was established in 1961 and the first laboratory in the field was set up in 1968. There was a need for the first Finnish clinical physiologists to get specialist training in the birthplace of clinical physiology.

The comprehensive laboratory of clinical physiology in Uppsala Academic Hospital offered a good place for three Finnish young doctors to be educated in the field. Under the guidance of professor Gunnar Ström, Arto Uusitalo started in 1967. Before the Uppsala period, Uusitalo had defended his doctoral thesis at the University of Helsinki, Institute of Physiology. After more than 2 years in Uppsala, he moved to Tampere, where he established the Laboratory of Clinical Physiology in the Central Hospital, based on Swedish principles. Uusitalo was soon nominated as the chief physician of that laboratory, the first in Finland. Later, in 1984, he became the first professor of clinical physiology in Finland at the University of Tampere.

Ritva Tammivaara also trained in clinical physiology in Uppsala during the years 1967–1971. She even defended her doctoral thesis in Uppsala but soon returned to Turku, where also specialised in pulmonary medicine. Tammivaara later served in 1988–1992 as the chief physician of clinical physiology at Kiljava Hospital in southern Finland.

Based on his positive experience, Uusitalo recommended Uppsala as an education place also to Anssi Sovijärvi, who had defended his thesis in 1973 at the Institute of Physiology in Helsinki. Sovijärvi wanted to specialise according to the Swedish model. He served as an assistant physician in 1975–1976 under the guidance of professor Ström. He completed specialist training in 1976 and was nominated as an associate professor in the same year at the University of Helsinki. After 5 years serving in Uusitalos laboratory in Tampere, he was nominated in 1982 as the first chief physician of clinical physiology at the Helsinki University Hospital and in 1994 as the first professor of clinical physiology at the University of Helsinki.

In Malmö, in the Laboratory of Clinical Physiology at the General Hospital, Esko Länsimies, who had recently defendend his PhD thesis in Turku, visited as a post-doctoral student in 1975 for 1 year. After this period, he was nominated as the chief of the Laboratory of Clinical Physiology at the Kuopio University Hospital in Eastern Finland. Later in 1998, he was nominated as the first professor of clinical physiology at the University of Kuopio.

Later at the beginning of the 1990s, Dr. Ari Lindqvist from Turku completed training in clinical physiology in 1992 at Lund University. Afterwards, he moved to Helsinki University Hospital to serve in administration and as the head of a research unit of pulmonary diseases.

Finnish physicians educated in Sweden in 1970s contributed essentially to the development of clinical physiology in Finland. They implemented in Finland several methods which already were in clinical use in Sweden. These include modern bicycle exercise test with Swedish reference values developed by associate professor Lars-Olof Nordesjö and with the scale of rate of perceived exertion (RPE) developed by professor Gunnar Borg. A short orthostatic test before exercise was also implemented for assessment of functional ECG changes.

The Finnish Society of Clinical Physiology nominated the following Swedish professors as honorary members based on their merits in science and in teaching Finnish physicians: Gunnar Ström from Uppsala, Sven-Eric Lindell from Lund and Håkan Linderholm from Umeå.

1.4 | The development of hospital laboratories of clinical physiology

Clinical physiology units evolved from clinical laboratories so that diagnostic activities in specific areas began to expand into new areas of clinical physiology that lacked diagnostic services. This diversification allowed the formation of a laboratory specialising in clinical physiology. In some hospitals, clinical physiology studies used to be part of the central laboratory's activities. As the activities expanded and reoriented within the hospital, there was a segregation of independent laboratories by the field. Such development occurred also in the field of clinical physiology. The key personnel were, in particular, specialists in clinical physiology who had received training in Sweden.

In Tampere, the medical management of the central hospital had found it necessary to establish a clinical physiological laboratory according to the Swedish model, and from the very beginning, there was a need to train a specialist in the field with the aim of acquiring specialist expertise for the new unit. The operation of the laboratory was started under the leadership of Arto Uusitalo on the basis of the former cardio-respiratory research department and by expanding the activities to include clinical physiological examinations performed within the framework of the central laboratory.

In Turku, the development of the specialty into a hospital began with the pioneering work of the Cardiorespiratory Research Unit, the Sports Medical Research Unit and the Department of Pharmacology of in Turku University. The Laboratory of Clinical Physiology was established in connection with the central laboratory in 1968. Heikki Wendelin was appointed first as an acting specialist and in 1976 he was nominated the first chief physician of the department.

When the University of Kuopio started its operations in 1972, the former Kuopio Central Hospital got university hospital status. With the development of the hospital and various methodological expansions, certain activities of clinical physiology and nuclear medicine under the central laboratory were merged into a new laboratory of clinical physiology and nuclear medicine, which was headed by Esko Länsimies.

In Helsinki, the formation of the Laboratory of Clinical Physiology was more complicated. Already in the early 1960s, there were plans to have a specialist position in clinical physiology for Eva Hirsjärvi in the laboratory at Kivelä Hospital in Helsinki. This plan was supported by the chief of the laboratory, Franz-Eduard Krusius, and also by the professors of cardiology and lung diseases. Unfortunately, a nation-wide strike of physicians ruined this plan. Later, the professor of physiology, Eeva Jalavisto, planned to establish a clinical physiology

laboratory in the new Helsinki University Hospital building, Meilahti Hospital, which was opened in 1965. However, this led to the formation of two different laboratories: a cardiac research laboratory in the Department of Medicine and a pulmonary function laboratory in the Department of Lung Diseases. The laboratory of clinical physiology developed above all after the expansion of the lung function laboratory to include physiological measurements of some other organ systems also. In 1986, the unit was renamed the Laboratory of Clinical Physiology with Anssi Sovijärvi as chief physician of the department.

In Northern Finland, Oulu University Hospital relies on clinic laboratories and does not have Laboratory of Clinical Physiology. Physiological cardiorespiratory measurements in Oulu University Hospital are accomplished in special laboratories of each clinic. Unit of Nuclear Medicine in Oulu University Hospital is currently part of the Department of Radiology.

In addition to the five university hospitals, there are 16 central hospitals in Finland. Their first specialists in clinical physiology started working in Pori (1977), Hämeenlinna and Joensuu (1982). Altogether, 11 central hospitals have had a laboratory of clinical physiology and nuclear medicine under guidance of the specialist in clinical physiology (and nuclear medicine). Unfortunately, five central hospitals have not been able to recruit specialists in the field. Moreover, as the first generation of specialists have recently retired, there are an additional four central hospitals today without permanent specialists. In most of these, university departments of clinical physiology or private specialists and private companies provide telemedical services or part-time consultations.

Moreover, some other hospitals, for example, Helsinki City Hospital, have had clinical physiology laboratories, but have later been incorporated into university hospitals.

In addition to hospitals, clinical physiology is an active part of the Finnish Institute of Occupational Health and the Center of Military Medicine in Helsinki, the UKK Institute in Tampere (which promotes health-enhancing physical activity) and six centers of sports medicine. In larger cities, there are also smaller private clinical physiology laboratories.

1.5 | New specialty of clinical physiology and nuclear medicine

Since 1978, clinical physiology had two subspecialties: paediatric clinical physiology and nuclear medicine, the latter of which was also a subspecialty in clinical chemistry and radiology.

In 1995, the Ministry of Education nominated a committee to reduce the number of medical specialties and subspecialties in Finland. At that time, there were 92 specialties and numerous subspecialties. In 1999, the committee reduced the number of main specialties to 49, and ended all subspecialties. Then the new specialty of clinical physiology and nuclear medicine was established in Finland.

Later, four universities started a 2-year programme of further training in molecular and hybrid imaging, and universities in Turku, Helsinki and Kuopio also in cardiovascular imaging.

1.6 | The status in universities developed slowly

Already before clinical physiology laboratories were established in hospitals, clinical physiology was a part of physiology courses in basic medical education in universities both in Helsinki and Turku and later also in Oulu. This was based on the fact that many of the teachers had specialised in clinical physiology. After clinical physiology laboratories were set up in hospitals and the number of specialists increased, the specialty gradually had more impact in clinical work. Subsequently, its role in the medical curriculum also became more important. The first hospital-educated specialists are presented in Table 1. Most of them had carried out their PhD research in the departments of physiology. After serving in hospital departments of clinical physiology, many of them were appointed as assistant professors in the field. This ensured the necessary number of

TABLE 1 The first hospital-educated specialists in clinical physiology (specialist's name, year of specialisation, the main training site)

Arto Uusitalo	1968	Uppsala
Ritva Tammivaara	1971	Uppsala
Heikki Wendelin	1972	Turku
Antti Viljanen	1972	Helsinki
Ilkka Vuori	1973	Turku
Olli Korhonen	1974	Helsinki
Asko Seppänen	1974	Tampere
Esko Länsimies	1975	Turku and Malmö
Yrjö Salorinne	1975	Helsinki
Pekka Halttunen	1976	Helsinki
Anssi Sovijärvi	1976	Helsinki and Uppsala
Juha Karvonen	1976	Tampere
Risto Härkönen	1976	Turku
Jaakko Hartiala	1979	Turku
Kari Antila	1979	Turku
Eino Hietanen	1979	Turku
Markku Saraste	1979	Turku
Lauri Pöyhönen	1980	Tampere
Lauri Laitinen	1980	Helsinki
Lauri Karhumäki	1981	Tampere
Väinö Turjanmaa	1982	Tampere
Barbro Sjövall	1982	Helsinki
Hannu Karanko	1982	Turku
Pertti Oinonen	1983	Turku
Pekka Varjo	1985	Turku
Olli Wanne	1985	Turku

university teachers. At the same time, education advanced to a clinical phase, mainly in disciplines of paediatrics, internal medicine, cardiology and lung diseases, as the discipline of clinical physiology was established later.

The hospital laboratories have modern equipment, which promoted multidisciplinary research. As a consequence, clinical physiologists networked with other clinicians in a fruitful collaboration. Today, they are at the top of research activity in their universities.

The chief physicians of four university clinical physiology departments were in charge of education in medicine at their universities. To coordinate basic and specialist education, they began annual meetings to plan education. This yielded the first two Finnish textbooks of clinical physiology in 1988 and in1994 and later three textbooks of clinical physiology and nuclear medicine in 2003, 2012 and in 2018.

Arto Uusitalo was nominated the first professor of clinical physiology in Tampere University in 1984. The first professor in Helsinki was Anssi Sovijärvi 1994, in Kuopio Esko Länsimies in 1998 and in Turku Jaakko Hartiala in 2003. Today the professors of clinical physiology and nuclear medicine formulate the rules for specialist training and are examiners of nationwide specialty examinations.

2 | FINNISH SOCIETY OF CLINICAL PHYSIOLOGY

2.1 | Founding and the first years

The technological advances in the field of laboratory medicine led to scientific specialisation and separation from other medical fields in the 1950s. The trend towards specialisation in the laboratory field led to increasing separation of scientific societies in 1970s. In Finland, joint national and Nordic congresses together with all laboratory fields were still organised, but at the same time, there was pressure from Sweden to establish a separate society for clinical physiology. Finally, a decision was made to found the Finnish Society of Clinical Physiology in 1975. Altogether 10 young experts from the field of clinical physiology participated in the founding meeting, which was held on 7 November 1975 in Helsinki, Meilahti Hospital. The chair of the meeting was Arto Uusitalo, who was also nominated as the first chairman of the new society. The by-laws for the society were established in this meeting, and the first official letter of the society, signed by Arto Uusitalo and secretary Heikki Wendelin, was addressed to the Swedish Society of Clinical Physiology, to announce the inception of neighbour society, and in the wish for good collaboration.

The main goals and means of the society were to support the development of clinical physiology and related sciences in Finland, by organising scientific meetings, collaborating with other national and international scientific societies, publishing-related literature, and giving information and statements to public authorities, institutions and other societies. The latter goal was very important, since in the 1970s, clinical physiology as a specialty was fairly unknown to many in the field of medicine.

The main actions during the first years of the society included statements to the National Medical Board and Finnish Medical Association concerning the position of clinical physiology in Finnish hospitals, and the planning of a specialty programme at the request of the National Medical Board. For the medical faculty in Helsinki University, a statement was sent to improve specialty training of clinical physiology, including a wish for the founding of the professorship. Scientific symposia were organised to launch this young specialty among other medical colleagues. The title of the first symposium in 1977 was 'Orthostasis', and included presentations by foreign speakers such as Olav Thulesius from Växjö and Sture Bevegård from Stockholm. Traditional national symposia were organised annually. Collaboration with other Nordic societies was close with continuous correspondence and participation in Nordic meetings and in editorial boards of scientific journals.

The following years in the 1980s were very productive under the leadership of Heikki Wendelin and Anssi Sovijärvi. The field of clinical physiology gradually took root as a specialty among others, as major actions were carried out to clarify the identity of the field and to improve the conditions of university training in medical faculties. These steps included a comprehensive report for the Ministry of Education in 1980, including characterisation of the impact of clinical physiology as a specialty in health care, contents of university training, and future needs for specialists. The society also coordinated the planning of specialisation programmes in different universities and units, and actively took part in Nordic collaboration when the Scandinavian Society of Clinical Physiology was founded in 1980 and the journal Clinical Physiology was established in 1981.

The organisation of the 4th Scandinavian Congress of Clinical Physiology in Turku 1983 was also a great effort and success. During the time of Anssi Sovijärvi as chair, the first steps for the Finnish textbook of clinical physiology were taken and a special issue of clinical physiology was published in the national journal Duodecim in 1984. In 1985, the society made also efforts to put pressure on the specialisation section of the National Medical Board to enhance education and training in clinical physiology. As a result, a special section was established (Raimo Vasama from the Medical Board as chair, professor Arto Uusitalo, associate professor Anssi Sovijärvi, associate professor Esko Länsimies and associate professor Jaakko Hartiala as members), presenting outlines and demands for university teaching and training in clinical physiology, which were in use until late 1990s. The chairmen and secretaries of the Finnish Society of Clinical Physiology and the years they held their positions are listed in Table 2.

2.2 | The specialty fights for existence

In the beginning of the 1990s, there were altogether 92 medical specialties in Finland. In 1995, the ministry of education coordinated a working committee to decrease the number of specialties, with

TABLE 2 The chairmen and secretaries (years) of the Finnish Society of Clinical Physiology

Chairman	Secretary
Arto Uusitalo (1975–1978)	Heikki Wendelin (1975–1978)
Heikki Wendelin (1978–1983)	Anssi Sovijärvi (1978–1981)
Anssi Sovijärvi (1983–1986)	Pekka Halttunen (1981–1983)
Esko Länsimies (1986–1988)	Juha Karvonen (1983–1986)
Yrjö Salorinne (1988–1990)	Lauri Karhunmäki (1986–1988)
Jaakko Hartiala (1990–1991 and 1993–1995)	Esa Ahonen (1988–1993)
Väinö Turjanmaa (1991–1993)	Tapani Parviainen (1993–1996)
Kari Antila (1995–1997)	Jukka Laitinen (1996–1998)
Esa Ahonen (1997–1999)	Hanna Mussalo (1998–2000)
Markku Walamies (1999–2001)	Mika Kähönen (2000–2001)
Vesa Järvinen (2001–2003)	Harri Lindholm (2001–2004)
Pekka Varjo (2003–2006)	Maria Juusela (2004–2006)
Hannu Koivu (2006–2009)	Kirsi Timonen (2006–2009)
Antti Loimaala (2009–2011)	Tomi Laitinen (2009–2012)
Päivi Piirilä (2011–2013)	Tuula Janatuinen (2012–2016)
Kirsi Timonen (2013–2016)	Saara Sillanmäki (2016–2019)
Pekka Malmberg (2016–2018)	Tuomo Tompuri (2019–)
Petri Haapalahti (2018–2020)	
Petri Kallio (2020–)	

professor in surgery Juhani Ahonen as the chair. By chance, professor Anssi Sovijärvi who was the head of the Laboratory of Clinical Physiology in Helsinki University Hospital, received information of the preliminary plans of the working committee, which included the elimination of clinical physiology from the list of official specialties in Finland. Anssi Sovijärvi acting as an initiator, an emergency meeting was organised in Helsinki together with professors Juhani Aaltonen, Arto Uusitalo, and associate professors Jaakko Hartiala, Väinö Turjanmaa and Esko Länsimies. Based on these intense discussions, a statement to ministry of education was composed, to clarify the position as a specialty in Nordic countries, and the clinical and scientific importance of clinical physiology and nuclear medicine in Finland. This statement was signed by professors Anssi Sovijärvi and Arto Uusitalo, and the representatives of the Finnish Society of Clinical Physiology and Section of Clinical Physiology in the Finnish Medical Association, Kari Antila and Väinö Turjanmaa.

The process lasted for 4 years, until the law for medical specialisation was changed. Although the number of specialties in Finland decreased from 92 to 49 and all the subspecialties were abolished, a new specialty was established in 1999 and named 'clinical physiology and nuclear medicine'. The above statement and personal discussions with the members of the working committee of the ministry of education were of utmost importance for this favourable outcome.

2.3 | Educational activities

The organisation of scientific meetings was one of the most important activities of the society from the very beginning. This was especially important to increase general knowledge and interest for the new specialty among medical professionals. Annual meetings were often organised in collaboration with other scientific societies, and took place in Hotel Korpilampi, Espoo, near Helsinki. Associate professor Antti Viljanen was in charge of the planning for the first meetings in 1978–1981, which included themes of physiological aspects of ventilator treatment, cardiopulmonary eligibility for surgical operations, respiratory function testing and assessment of chest pain. Traditionally, the meetings also included exhibitions by the representatives of medical industry, a sauna and a dinner with dance music, in this order.

Due to the economic depression in the 1990s, the number of participants in the meetings decreased. Korpilampi was also regarded as outdated as a conference place, and in 2000, the venue for annual meetings was changed to the Hanasaari Conference Center in Helsinki. Since 2005, the venue for annual meetings has varied between different university cities in Finland. These meetings were given nicknames according to local dialect such as 'Nysse'-days (in Tampere), 'Föri'-days (in Turku) or 'Veljmiespäevät' in Kuopio. State of the art lectures have been included in the traditional programme since 2011, the original idea being invited presentations by experts from Finland and abroad.

The Finnish Society of Clinical Physiology has also been active in organising other educational programmes in Finland, such as those in National Doctor Days and Labquality Days, and symposia for specific topics. In these events, collaboration with other scientific societies and representatives of medical industry has been fruitful.

2.4 | Textbooks of clinical physiology in Finland

At the time when the specialty of clinical physiology was established in 1965, there were no Finnish textbooks available. The classic textbook 'Clinical Physiology' by Torgny Sjöstrand was used as a reference during training. In the beginning of 1980s, the Finnish Society of Clinical Physiology set the goal of writing a Finnish textbook to strengthen the position of the field in Finland. However, first it was important to train a sufficient group of experts for central hospitals and laboratories. Many of the trainees got their education and expertise from Sweden. In 1985, when Arto Uusitalo was nominated as the first professor in Tampere University, it was clear that he should take the leading role in the textbook project. The pharmaceutical



FIGURE 1 Writers of the first Finnish textbook of clinical physiology: From the back left: Esa Ahonen, Pertti Oinonen, Lauri Karhumäki, Esko Länsimies, Risto Härkönen; from the front left: Olli Wanne, Pekka Varjo, Arto Uusitalo, Jaakko Hartiala, Yrjö Salorinne and Anssi Sovijärvi

company Orion agreed to act as a publisher, and professor Arto Uusitalo was chosen as the chief editor. Other editors in this first textbook were associate professors and chief physicians of clinical physiology, Anssi Sovijärvi from Helsinki, Esko Länsimies from Kuopio, and Ilkka Vuori from Tampere (Figure 1). The conception of the first Finnish textbook including 600 pages was a huge project, which took several years. However, this piece of work had an important impact on the establishment of the field among other specialties.

The textbook of clinical physiology has been updated regularly after the 1980s. These textbooks have been published by Duodecim, with professor Anssi Sovijärvi acting as the chief editor. The textbook published in 2003 was entitled 'Kliininen fysiologia ja isotooppilääketiede' and included up-to-date articles in both clinical physiology and nuclear medicine, according to the newly established specialty. The last updated textbook was published in 2018, with the editorial board consisting of Anssi Sovijärvi (chief editor), Jaakko Hartiala, Juhani Knuuti, Tomi Laitinen and Pekka Malmberg. The textbooks have served as flagships of the specialty in Finland and have been valuable in both specialty training and basic education of medical students and other health professionals working in the field of clinical physiology in Finland.

2.5 | General meetings and awards

Annually, the Finnish Society of Clinical Physiology has organised statutory general meetings with official agenda, traditionally at spring time. During the first years after its founding, there were only few members in the society, and cocktail parties were hosted by local colleagues at their homes. Spouses were also invited. This tradition was no longer possible when the society grew in number of members. The meetings have also included a scientific programme, in the beginning by experts of current specific topics and lately by young specialist trainees and doctoral students in the field of clinical physiology. The castle of Turku has been the venue for many 10-year annual celebrations. In 2006, the 30th annual meeting was celebrated in Forum Marinum, Turku Figure 2.

Since 1985, the board of the society has traditionally granted young scientists in the field of clinical physiology with a stipend named after Heikki Wendelin. Annually since 1986, it has been also customary to acknowledge colleagues that have served for the benefit of clinical physiology, that is by actively working in the board of the society. Special awards have been granted for methodological development in the field of clinical physiology. These grants have been named after pioneers of the field, such as Arto Uusitalo Prise, Anssi Sovijärvi Prise and Esko Länsimies Prise. The society has also financially supported young trainees and scientists for their professional development by travel grants.

2.6 | Scandinavian congresses in Finland

One of the important tasks for the national society has been to support and organise scientific congresses in Finland, in collaboration with the Scandinavian Society. The 4th Scandinavian Congress of Clinical Physiology was organised by the Finnish Society of Clinical Physiology and Rehabilitation Research Centre of the Social Insurance Institution of Finland, in Turku 1983. Associate professor Heikki Wendelin, the chairman of the national society, acted also as the president of the congress, and the honorary president was chancellor Kaarlo Hartiala from the University of Turku. Other members of the organising committee were professor Heikki Frick from Helsinki, professor Leo Hirvonen from Oulu, Anssi Sovijärvi from Helsinki and professor Arto Uusitalo from Tampere. The congress was a success for the small field in Finland, with over 130 active participants from six countries. Invited lecturers included professor Nils-Holger Areskog from Sweden (Autonomic nervous system), Dr. E.B. Raftery from Great Britain (Long-term registrations), Professor N.A. Lassen from Denmark (Radioisotopes in lung



FIGURE 2 In 2006, the 30th annual meeting of the Finnish Society of Clinical Physiology was celebrated in Forum Marinum, Turku. The photo is taken in front of Daphne, the sailboat of novelist Göran Schildt in his journeys in the Mediterranean Sea. From the left: professors Esko Länsimies, Yrjö Salorinne, Arto Uusitalo, Ilkka Vuori and Anssi Sovijärvi

function diagnostics) and professor Pentti. M. Rautaharju from Canada (New techniques in electrocardiography). Based on the revenue from the exhibition in this congress, a fund named after Heikki Wendelin was founded to support young scientists in the field of clinical physiology in Finland.

The following international congress in Finland was organised in Helsinki 1989. The VIII Scandinavian Congress of Clinical Physiology was scheduled together with the XXXI International Congress of Physiological Sciences (president chancellor Kaarlo Hartiala). The president of the Nordic congress was associate professor Anssi Sovijärvi from Helsinki, and the secretary general was associate professor Yrjö Salorinne. Over 2000 scientists participated in the international congress, and the Scandinavian congress had over 150 active participants.

Collaboration between organisers and societies in the field of clinical physiology and nuclear medicine increased during 1990s, and when Finland was in turn to be in charge of the next Scandinavian congress in 1998, it was decided to organise a joint meeting of the XI Scandinavian Congress of Clinical Physiology and the III Nordic Congress of Nuclear Medicine in Helsinki. The organisers of the joint meeting were the Finnish Society of Clinical Physiology, the Finnish Society of Nuclear Medicine, and the Nordic Societies of Clinical Physiology and Nuclear Medicine, and it was supported by the International Union of Physiological Sciences. The president of the joint congress was professor Anssi Sovijärvi, who was also the chairman of the Scandinavian Society of Clinical Physiology at that time. Associate professor Yrjö Salorinne acted again as the secretary general. The venue for the Congress was Marina Congress Center in downtown Helsinki, and over 250 scientists took part in the event. High-quality review presentations were given by 14 invited distinguished scientists from the Nordic countries, USA, Canada, Germany and Holland. Scientifically and financially, the congress was a great success.

TABLE 3 Honorary members of the Finnish Society of Clinical Physiology

Gunnar Ström, Uppsala (1983)
Håkan Linderholm, Umeå (1983)
Tuomas Peltonen, Turku (1984)
Kaarlo Hartiala, Turku (1984)
Arto Uusitalo, Tampere (1986)
Leo Hirvonen, Oulu (1987)
Pentti Siltanen, Helsinki (1988)
Martti J. Karvonen, Helsinki (1993)
Dwain L. Eckberg, Richmond VA (2000)
Esko Länsimies, Kuopio (2004)
Yrjö Salorinne, Helsinki (2004)
Anssi Sovijärvi, Helsinki (2009)
Jaakko Hartiala, Turku (2016)
Väinö Turjanmaa, Tampere (2020)

2.7 | Honorary members of the Finnish Society of Clinical Physiology

The Finnish Society of Clinical Physiology has nominated especially distinguished actors in the field of clinical physiology as honorary members. The board of the society proposes the nomination, and the final decision is made by the general meeting. Professor Arto Uusitalo is the only person who has been nominated as the honorary chairman, in 1995. The honorary members and the years of nomination are listed in Table 3.

3 | DEVELOPMENT OF CLINICAL PHYSIOLOGY IN HELSINKI UNIVERSITY HOSPITAL AND SURROUNDING REGIONS

3.1 | Helsinki and Helsinki University

Helsinki, the capital of Finland, was founded by the Swedish king Gustav Vasa in 1550 at the mouth of the river Vantaa on the south coast of Finland. The city was replaced more south on the Helsinki pensinsula in the 1600s, where it started to grow rapidly. After the Finnish War in 1808–1809 between Sweden and Russia Finland was annexed to Russia as an autonomous Grand Dutchy in 1809. Helsinki was proclaimed the Finnish capital in 1812, and in 1828 Finland's first university, which had been founded in Turku in 1640 as the Royal Academy of Turku, was transferred 'en bloc' to Helsinki, also including the faculty of medicine. Then it was renamed Imperial Aleksander University.

For university teaching of medicine, the Clinical Institute of Helsinki was established in the year 1833. At that time there were three professors in the faculty of medicine, one of those for anatomy and physiology. As Finland became independent in 1917, the university was renamed again, as the University of Helsinki. The first professor in physiology was Robert Tigerstedt starting in 1900. He had written the internationally acknowledged textbook of physiology, 'Lehrbuch der Physiologie des Menschen I und II'. Together with a Swedish colleague, R. G. Bergman, he discovered renin, the main regulator of circulation of kidneys. Another great physiologist at the University of Helsinki was professor Ragnar Granit, who received the Nobel Prise in 1967 based on his studies on neurophysiology of muscles and vision. Based on their work in the beginning of the 1900s with marked contributions by professors Yrjö Reenpää, Eeva Jalavisto and Matti Bergström at the Institute of Physiology, the importance of physiology for clinical problems was widened.

The discipline of clinical physiology was established in Finland in 1961. In the 1970s, the intention to get a professor chair for clinical physiology was discussed for the first time in the Faculty of Medicine at the University of Helsinki. However, it lasted over 20 years till the first professor chair of clinical physiology was established in Helsinki. Anssi Sovijärvi, associate professor and chief physician of clinical physiology at Helsinki University Hospital, was invited to the post in 1994.

3.2 | Founding of Helsinki University Hospital

A law on university hospitals was accepted in the Finnish parliament in 1957. Based on that law Helsinki University Hospital was founded in 1958 when Helsinki General Hospital and the Hospital of Red Cross were joined together. Helsinki General Hospital was a combination of several separate hospital buildings and clinics, the oldest ones situated in the cape of Helsinki and one in the Lapinahti area on the west coast of the cape of Helsinki, and the newer ones in the Meilahti hospital campus area. When Helsinki University Hospital was founded, altogether 15 different clinics existed. The heads of the hospitals were university professors.

Because the old clinics were geographically very scattered, a project to build a new large hospital in the Meilahti campus area was started. The new university hospital, Meilahti Hospital was completed in 1966. It consisted of three clinics of medicine, two clinics of surgery, departments of neurology, radiology, clinical laboratory and a department of pulmonary medicine. At that time the clinics had their own laboratories for physiological studies. Non-invasive and invasive physiological heart studies were performed in the cardiac laboratory, which was a part of the Department of Cardiology. The new Department of Pulmonary Medicine in Meilahti hospital also had a lung function laboratory, which then later developed and enlarged into the first Laboratory of Clinical Physiology at Helsinki University Hospital.

3.3 | Lung function laboratory of Helsinki University Hospital 1966–1981

Associate professor Håkan Poppius (Figure 3), a specialist in pulmonary diseases, was invited to take responsibility for the new lung function laboratory at Meilahti Hospital. He had previously set up a very qualified lung function laboratory in Laakso Hospital,



FIGURE 3 Professor Håkan Poppius

one of the municipal hospitals of Helsinki city. Poppius was dedicated to developing a laboratory with modern medical technology to reach a high international level. With the help of associate professor Antti Viljanen, specialist in clinical physiology and pulmonary diseases, the following methods were validated for clinical use: flow-volume spirometry, bronchial hyperactivity (BHR) test with inhaled histamine (Cockroft method), clinical exercise test with arterial blood gas analysis, capnography of exhaled air, single-breath diffusing capacity test (Cotes method), constant volume body plethysmography (Siemens body box), Xe-133 radiospirometry with two moving detectors, nitrography with determination of closing volume, testing of exercise-induced asthma with cold air inhalation and determination of anatomic right-to-left shunt with inhalation of 100% oxygen. In the laboratory also the first versions of ear oximeters were tested (Hewlett-Packard), but they did not show reliable results.

Several young physicians trained in Poppius' laboratory to understand clinical lung function studies for specialisation in clinical physiology. Those included Yrjö Salorinne, Lauri A. Laitinen, Pekka Halttunen, Barbro Sjövall and Anssi Sovijärvi. In the beginning of the 1980s associate professor Antti Viljanen, with the help of Pekka Halttunen, published new Finnish reference values for flow-volume spirometry, body plethysmography and single-breath diffusing capacity in never-smoking adults. These values were soon implemented for clinical use in Finland. The spirometry values were much higher than the older values by Berglund from Sweden, the material of which included also smokers. During the period of Poppius, the laboratory acquired the Valmet BI-1200 multidetector radiospirometer at the end of the 1970s for the measurement of regional lung function.

Håkan Poppius was selected as professor of pulmonary diseases in 1981 at the University of Helsinki. Thereby, the position of chief physician of the lung function laboratory was declared for open application at the beginning of 1982.

Three specialists in clinical physiology were interested: Antti Viljanen, Lauri A. Laitinen and Anssi Sovijärvi. The youngest of the applicants, Anssi Sovijärvi was chosen for the position, which he held for over 30 years. He started his work as the chief physician with great enthusiasm, and the laboratory developed quite rapidly into a big unit of clinical physiology.

Associate professor Antti Viljanen moved soon from the specialist position of the lung function laboratory to Meltola hospital, earlier a west Nyland sanatorium of tuberculosis, where he set up a modern laboratory of clinical physiology and nuclear medicine, Lauri A. Laitinen established the Institute of Military Medicine in Helsinki in 1984, where he served as its head for several years and after some years in Sweden as a research manager for Astra-Draco. Laitinen was then selected as the professor of pulmonary diseases after Poppius in 1992, and in 1999–2006 he served as the general manager of HUS—Helsinki University Hospital.

3.4 | Development of the lung function laboratory into a full-service laboratory of clinical physiology

3.4.1 | Educational approach for training of clinical physiologists in the 1980s

As there were no training positions at Helsinki University Hospital for clinical physiology, Sovijärvi planned a rotating training programme. An assistant physician of the lung function laboratory served in several clinic laboratories for several months each, like in the cardiac laboratory of the Department of Cardiology, in the angiolaboratory of the Clinic of Surgery, in the gastroenterology laboratory of the Department of Medicine, in the urologic laboratory of Meilahti Hospital, in the cardiorespiratory function laboratory of the Allergy Hospital and in the units of nuclear medicine of Meilahti Hospital. The assistant physicians could also get part of the necessary training in the lung function laboratory of Laakso Hospital, in the function laboratories of the Institute of Occupational Health, the Institute of Military Medicine and a private hospital (Diakonissalaitos).

3.4.2 | Discipline of clinical physiology established at the University of Helsinki and Helsinki University Hospital in 1986

The lung function laboratory started new methods like ambulatory blood pressure recording, function tests for assessment of the autonomic nervous system, ambulatory ECG recordings, and tests of peripheral circulation during rest and exercise. All studies of the laboratory were since 1986 available for patients from any clinic and some of them also for patients in the basic health service of the city of Helsinki. Thus, the Swedish idea of a central laboratory service was fulfilled.

In 1986, clinical physiology was accepted as an independent educational discipline for medical students. The teachers at that time were associate professors Anssi Sovijärvi and Yrjö Salorinne.

3.4.3 | Methodological development since 1982

The Finnish reference values of flow-volume spirometry, single-breath diffusing capacity and body plethysmography were published by Viljanen et al in 1982, but the classification of decreased values were not yet established. Sovijärvi calculated for Finnish guidelines the percentage limits of slight, moderate, severe and very severe decrease of all lung function variables based on the standard deviation (SD) units of each variable in the healthy reference population over 30 years before the ATS/ERS guidelines implemented the use of *z*-values of the variables in each age group.

The quality of spirometry and peak expiratory flow measurements were markedly improved in Finland by Finnish guidelines about how to measure and interpret these studies. Since 1995,

up-dated versions of the guidelines were regularly delivered, the newest one in 2021 (15th edition) under the leadership of Sovijärvi.

Computerised lung function and ECG devices started to come out at the beginning of 1980s. Computerised spirometers with flow transducers, volumetric spirometers, single breath diffusing capacity devices and constant volume body plethysmograph were acquired from Erich Jaeger GmbH in Germany. Calculation of non-ventilated lung compartment was applied for clinical use. Computerised exercise ECG was also soon applied.

Clinical physiology also contributed in diagnostic sleep apnoea studies by using a static charge-sensitive bed (SCSB) and pulse oximeter. SCSB and transient sound recording by the aid of a paraboloid mirror were used for quantitative recording of cough. This invention was used to test new antitussive drugs. The computer programmes for the studies with SCSB were compiled by clinical neurophysiologist Tapani Salmi. The European Respiratory Society (ERS) guidelines of Chronic Cough in 2004 noted this unique method.

In 1986, the laboratory set up a new computerised exercise testing system with continuous gas exchange analysis, a spiroergometer test. This test produced a variety of gas exchange variables and was used for all patient studies when assessing the limitations of exercise tolerance and reasons for dyspnoea. It has been since then the basic method to assess circulatory and respiratory limitations, including increased work of breathing in obesity or in pulmonary obstruction or stiffness. The 12-lead ECG during exercise were modified by adopting the Mason-Likar system for placement of the electrodes.

Gas exchange analysis was also adopted in orthostatic tests for assessing hyperventilation syndrome and in exercise tests with arm cranking. For both tests, the laboratory published reference values, which still are in clinical use.

At the end of the 1980s, Sovijärvi started to develop new sensitive diagnostic methods for asthma. One new method was a rapid dosimetric method with controlled tidal breathing for assessment bronchial hyperreactivity (BHR) to histamine. The result was obtained in terms of provocative dose of histamine inducing a decrease of FEV1 by 15% from the baseline (PD15FEV1). According to findings in a large clinical material, its sensitivity and specificity for asthma with certain PD15FEV1 values were determined. According to international comparisons, the method showed superior repeatability and reliability to assess BHR.

In the middle of the 1990s, two studies were published in Lancet that showed that the fraction of exhaled nitric oxide (FENO) was increased in asthma. The laboratory of clinical physiology rapidly bought a chemiluminescence NO-analyser and developed a computerised system to assess FENO during a defined expiratory flow. The first reference values of FENO were soon published by the laboratory and the method was applied for clinical use as the first laboratory in Finland 1996. Since then measurement of FENO has been included in clinical asthma testing in Helsinki University Hospital.

At the end of the 1990s, FENO measurements in Helsinki were used in a multicenter epidemiological research project between Finland, Estonia and Sweden (FinEsS). These data have been exploited even in 2020. Four academic dissertations about FENO in different phenotypes of asthma and allergy and about its epidemiology in Nordic countries were published from the laboratory of clinical physiology.

An original invention was the development of computerised lung sound analysis. The project was started at the beginning of the 1990s. The idea by associate professor Sovijärvi was to develop a computerised stethoscope. At the first stage patients of different types of crackles were recorded with sensitive microphones to be analysed at the Institute of Phonetical Sciences at the University of Helsinki. Research cooperation for over 10 years with the group of professor Toivo Katila from Helsinki University of Technology produced a computerised lung sound analyser HELSA (Helsinki Lung Sound Analyser) which could record, detect and analyse in real-time crackles and wheezes based on phonopneumogram, FFT-specra, frequency spectra in sonograms and superimposing them on flow-volume loops. Dr. Päivi Piirilä made studies on crackles and cough sounds in patients for her thesis (1992). The opponent was prof. Robert Loudon from the USA. Dr. Pekka Malmberg studied spectral characteristics of breath sounds in asthma and COPD for his thesis (1996). His opponent was prof. John Earis from Great Britain. The science carried out by the Helsinki group offered new knowledge of lung sounds for clinical use. Accordingly, the HELSA analyser was exploited in clinical problems.

The lung sound group at the Helsinki University of Technology produced several master thesis studies in engineering.

3.4.4 | EU project and ERS Task Force on computerised lung sound analysis

In the meetings of International Lung Sound Association in 1993 in Italy the works of the Helsinki Lung Sound group aroused positive attention. The Association decided to suggest a European project to produce recommendations for computerised respiratory sound recording and analysis and selected associate professor Anssi Sovijärvi to chair the group of lung sound researchers from seven European countries. The plan of the group was accepted as a concerted action project by the EU in its BIOMED frameworks and also ERS nominated the project as a Task Force of the Society in 1994. The product of the project was an ERS Task Force Report on 'Computerised Respiratory Sound Analysis (CORSA)', which was published in European Respiratory Review in the year 2000. The report included also recommendations for the nomenclature of respiratory sounds. The CORSA project supported further development of the HELSA device, especially as Doctor Jan Vanderschoot, one of the group members from Leiden University contributed to the basic science of respiratory signal processing.

3.4.5 | Professorship and chair of clinical physiology at Helsinki University

The Medical Faculty of the University of Helsinki had considered establishing a professorship and chair of clinical physiology already in 1960s, but due to lack of good candidates for the position the idea was not realised until 1994. Because associate professor Anssi Sovijärvi had set up the laboratory of clinical physiology in Helsinki University Hospital and the new university law in Finland made it possible to found part-time professorships, the medical faculty decided to establish a professorship and chair for clinical physiology in 1994. Associate professor Sovijärvi was invited to the post (Figure 4). Sovijärvi reformulated courses of clinical physiology for medical students and organised specialist education in clinical physiology. He retired from the professorship and the chief physician post in 2013. He was also the administrative head of the Laboratory of Clinical Physiology, which was combined later with the Laboratory of Nuclear Medicine in Helsinki University Hospital. After a long interregnum time his successor as professor became Päivi Piirilä in 2019 (Figure 5).



FIGURE 4 Professor Anssi Sovijärvi



FIGURE 5 Professor Päivi Piirilä

3.4.6 | International research projects after the middle of 1990s

In addition to the computerised lung sound group, the Laboratory of Clinical Physiology participated actively in two extensive international research projects where professor Sovijärvi had a leading position. In 1996, an epidemiological project on asthma, and allergy, COPD and respiratory symptoms was started together with Finland, Estonia and Sweden (FinEsS). The primus motor of FinEsS was associate professor, later professor Bo Lundbäck from Umeå and Gothenburg. The data collection of the project included also measurements of lung function, BHR and FENO from the general population. The research centers at the beginning were Helsinki, Kemi, Narva, Saaremaa, Stockholm, and Örebro and later also Seinäjoki and Vaasa.

The project is still continuing in an enlarged form. Norway is also involved, and the name has been changed to EpiLung. The project leader is now professor Eva Rönmark from Umeå. Professor Sovijärvi was during the first 30 years the coordinator in Finland, followed by professor Piirilä. Several lung specialists and clinical physiologists did their academic dissertations within the project, including Jyrki Kotaniemi, Annette Kainu, Paula Pallasaho, Heikki Ekroos, Annamari Rouhos, Maria Juusela and Paul Lassmann-Klee. Scientific collaboration in the project with Tari Haahtela, professor of allergology of Helsinki University, was very fruitful. The project has shown for example, that the prevalence of asthma has increased in Helsinki between the years 1996 and 2016 from 6% to 11%, but then levelled off and that there has been a west-east disparity of allergic diseases between Sweden, Finland and Estonia.

In 1998, the Laboratory of Clinical Physiology was involved in an experimental research project in Grenoble, where a big European research center for physics (ESRF) is located. The Finnish professor of physics Pekka Suortti asked professor Anssi Sovijärvi to lead the medical science branch in experimental pulmonary physiology. In the synchrotron laboratory the ventilation of rabbit lungs could be imaged with the accuracy of 0.1 cubic millimetre with the K-edge subtraction method using xenon gas. Several studies on experimental asthma revealed regional mechanisms of nonuniform distribution of

specific ventilation during asthmatic bronchoconstriction and, by using iodine, also changes of regional pulmonary perfusion. A very heterogeneous distribution of inhaled aerosol particles in the lungs of healthy rabbits was also a new finding. Professor Sam Bayat from Grenoble has been the key person in experiments and manuscript writing. Images of ventilation disturbances in an asthmatic rabbit were shown on the cover page of an issue of Respiratory and Critical Care Medicine from 2009. The scientific group consisted researchers from Switzerland, Hungary, France and Finland. Finnish physicists Liisa Porra and Satu Strengell completed their academic dissertations in the project.

3.4.7 | Reorganisation of Nuclear Medicine in Helsinki University Hospital in 2000

Since 1978 nuclear medicine was a subspecialty of clinical physiology in Finland until 1999. In that year, clinical physiology and nuclear medicine were combined to form a new principal specialty. In the first decades of the existence of Meilahti Hospital, founded in 1966, there were two units of nuclear medicine: the Laboratory of Nuclear Medicine in the central laboratory and nuclear medicine functions in the Department of Radiology. For both units, several gamma cameras were acquired in the 1970s, 1980s and 1990s.

A new hospital organisation, HUS (Helsinki University Hospital), was started in 2000. The facilities of clinical physiology and nuclear medicine were reorganised together in the Helsinki area. The Laboratory of Clinical Physiology in Meilahti Hospital was joined with the Laboratory of Nuclear Medicine, with facilities of nuclear medicine in the Department of Radiology in Meilahti, and with all facilities of clinical physiology and nuclear medicine of the hospitals in Helsinki, the Laakso, Maria and Malmi Hospitals. The administrative head of all these facilities was professor Anssi Sovijärvi. The head of the nuclear medicine branch from the year 2000 until 2012 was professor h.c. Aapo Ahonen and after him associate professor Antti Loimaala.

In 2004, the hospital organisation was changed again. The activities of clinical physiology and nuclear medicine in Jorvi Hospital (Espoo city), Peijas Hospital (Vantaa city) and Hyvinkää Hospital (Hyvinkää city) were also joined to clinical physiology and nuclear medicine as part of the University Hospital organisation. After this reorganisation, the discipline consisted of nine gamma cameras. All images produced by nuclear medicine and radiology have been stored in digital form (PACS) since 2002. Nuclear imaging of the heart during exercise was still possible also in the Department of Cardiology in Meilahti Hospital.

Clinical physiology increased service capacity for cardiology by improving the possibilities for long-term recordings of ECG and cardiac ultrasound studies. ECG recordings of the whole District of Newland (Uusimaa), inlcuding all hospitals and health centers, were put in the same database in digital form (Digi-ECG) using the MUSE programme by GE Healthcare. The system consisted also exercise and long-term recordings. Associate professor Petri Haapalahti was the manager of this development. The spirometric studies were also stored in digital form in a common database for all units in the Newland area.

An important milestone in nuclear medicine took place in 2006 when the first PET-CT camera (Philips Gemini GLX 16) of Helsinki University Hospital was installed. This was the first PET camera outside the National Turku PET center in Finland. Since then the activity of nuclear imaging has been more and more directed to PET imaging, and in addition to the classical 18-F-FDG new tracers were developed. Soon two new PET-CT cameras were implemented, Siemens Biograph 64 and GE Discovery MI PET-CT 128. For their own production of PET- tracers, the Unit of Nuclear Medicine received a cyclotron (IBA, 18 MeV). This device made it possible to produce short-lived positron emitters with O-15 used especially for heart studies.

In 2012, the hospital organisation of clinical physiology and nuclear medicine was changed again. The facilities were included as part of the Helsinki University Hospital Imaging Center. This change proved to be beneficial. After this change, specialists in radiology contributed to the interpretation of all PET-CT and SPECT-CT images.

In 2013, there were 18 specialist physicians, six junior physicians, five physicists, two radiochemists and 69 laboratory assistants in the field of clinical physiology and nuclear medicine.

3.4.8 | Specialist education

Between the years 1982 and 2019 Helsinki University Hospital was responsible for the education of 30 specialists in the field of clinical physiology and nuclear medicine. In addition, the Laboratory of Clinical Physiology offered side education for 50 physicians in pulmonary medicine, anaesthesiology or sports medicine. Supplementary education of molecular and fusion imaging was started at Helsinki University in the beginning of the 2010s.

3.5 | Clinical physiology in municipal hospitals of Helsinki city

Clinical physiology in the municipal hospitals of Helsinki started in the beginning of the 1960s in Laakso Hospital, which earlier served mainly as a sanatorium for pulmonary tuberculosis. In that hospital, pulmonary specialist Håkan Poppius, later professor of pulmonary diseases, developed an advanced lung function laboratory with the possibility of 17 different lung function and exercise studies. When Poppius was called to lead the lung function laboratory of the new Meilahti Hospital in 1965, the responsibility for lung function laboratory of Laakso Hospital was remained to a variety of lung specialists until 1979, when an expert in clinical physiology, Yrjö Salorinne, was nominated as the head of the laboratory (Figure 6). Between 1979 and 1999 the Laakso lung function laboratory, soon renamed the Laboratory of Clinical Physiology, served as a central



FIGURE 6 Professor Yrjö Salorinne

laboratory for all municipal hospitals of Helsinki, that is, the Laakso, Aurora, Kivelä, Malmi, Hesperia and Maria Hospitals. Those hospitals formed a regional hospital network for Helsinki.

In the 1990s, the Laakso clinical physiology was moved to new larger premises including facilities for gamma camera activity, and versatile cardiorespiratory studies. At that time clinical physiology offered over 50 different function studies for in and out-patients in Helsinki. In the 1990s two specialists, one physicist and seven laboratory assistants were employed in the Laakso Laboratory of Clinical Physiology. Associate professor Salorinne also helped the University Hospital in specialist education for forthcoming clinical physiologists since 1984. In 1992, gamma camera imaging in Maria and Malmi Hospitals was moved to the central laboratory in Laakso Hospital.

In 1996, all services of clinical physiology and nuclear medicine in the Newland area were graded between Helsinki University Hospital, Helsinki city hospitals, and Jorvi, Peijas, Hyvinkää and Meltola Hospitals. The basic clinical physiology like spirometry, diffusing capacity test, bicycle exercise, Holter ECG, and RR-24h recordings included in the repertoire of all laboratories but the most demanding investigations including nuclear medicine imaging only in Helsinki University Hospital and in some specialised laboratories. General physicians of all municipal health centers could send their patients to all basic studies of clinical physiology without consultation of a clinical specialist.

In the year 2000, all hospitals of Helsinki city and all University hospitals were joined to the same organisation, including all activities of clinical physiology and nuclear medicine. As a consequence, in 2005, all activities of clinical physiology and nuclear medicine was centralised from Laakso Hospital to Meilahti Hospital, where more space was obtained for transferred functions. This change took place concomitantly with the retirement of professor h.c. Yrjö Salorinne.

3.6 | Clinical physiology in other hospitals surrounding Helsinki

The **Hospital of Allergology** is situated close to Meilahti Hospital and became a part of the Helsinki University Hospital in 1970. In that hospital, the Laboratory of Clinical Physiology began in 1990, first by using consulting specialists from Meilahti Hospital and later, in 1992 a specialist post was established with the help of the hospital director, chief physician Tari Haahtela. The first specialist in clinical physiology was Heikki Tikkanen (later professor of sports and exercise medicine), followed soon by Jarmo Skyttä and Pekka Malmberg (associate professor since 2003).

During the long period under Malmberg, since 1996, the development of the laboratory was rapid. It focused on developing lung function studies for children and bronchial provocation tests in allergic airway diseases. Impulse oscillometry for assessment of lung function was introduced for clinical use by creating reference values in healthy children. The baby body-box, the first in Nordic countries, was exploited for assessment of airway problems in babies. The eucapnic hyperventilation test, spiroergometric tests and dosimetric methacholine provocation tests were validated. For assessment of eosinophilic airway inflammation fractional exhaled nitric oxide (FENO) test was validated for children. Some of the most recent innovations are ambulatory impedance pneumography for assessment of nocturnal asthma in children and video laryngoscope monitoring during exercise for assessment of vocal cord dysfunction. At the moment two specialists are working in this laboratory.

Jorvi Hospital, a new regional hospital for the West Newland area and especially for Espoo city, was established in 1976. Nuclear medicine was started soon after with a gamma camera, but the Laboratory of Clinical Physiology with all necessary services was established first in 1997. The first specialist and head of the laboratory was Jarl-Erik Nyholm, followed soon by Lauri Karhumäki. He received the position of chief physician in 1999. The unit included at that time two gamma cameras and a large variety of basic clinical physiology; exercise tests with gas exchange analysis and treadmill exercise test, Holter ECG, cardiac ultrasound imaging, myocardial perfusion studies with gamma camera, spirometry, impulse oscillometry for children, and pulmonary diffusing capacity and long-term pH studies of oesophagus as well as bone density measurements. The laboratory served all clinical units of the hospital. Nuclear medicine developed also rapidly in Jorvi laboratory. Especially sentinel node studies were actively performed since the beginning of 2000s. In 2001, Jorvi Hospital was joined to Helsinki University Hospital, and thus the Laboratory of Clinical Physiology and Nuclear Medicine became a part of the university hospital organisation.

Peijas Hospital was established in 1990 as the regional hospital of Vantaa city situated in the middle part of Newland

county. The Laboratory of Clinical Physiology began in 1992 together with clinical neurophysiology. However, the first specialist of the discipline, Heikki Tikkanen, was first recruited at the end of the 1990s. In 2000, this hospital was also joined to the Helsinki University Hospital organisation, and the first chief physician of clinical physiology, Markku Walamies, was nominated to the post. In 2007 the laboratory enlarged by getting new modern premises and more physician capacity. Besides basic cardiorespiratory function studies all function studies of the oesophagus and head-up tilt tests of Helsinki University Hospital were centralised to this laboratory. No nuclear medicine services have been planned for Peijas Hospital.

Kiljava Hospital served earlier since the 1950s as a sanatorium for tuberculosis, but its function was changed later to serve as a hospital for internal medicine and pulmonary diseases. The Laboratory of Clinical Physiology was established there in 1988, when associate professor Ritva Tammivaara was nominated as the chief physician. She set up a modern cardiorespiratory laboratory. In 1991, Tammivaara moved to Turku, and she was replaced by Vesa Järvinen (associate professor since 2021). who further developed the laboratory to also serve patients from the Lohja and Porvoo regional hospitals in West and East Newland. When the new building for **Hyvinkää Hospital** in North Newland was finished in 2001, it also included good facilities for clinical physiology but without nuclear medicine. The laboratory of clinical physiology was then moved from Kiljava to Hyvinkää Hospital, and a second chief physician, Heli Räty, was appointed. Järvinen had a very kean interest in cardiac ultrasound and MRI studies of heart as well as in exercise studies. The laboratory also developed high-quality sleep apnoea measurements. Hyvinkää Hospital was joined to the Helsinki University hospitals in 2008.

Meltola Hospital was originally a sanatorium for Swedish-speaking tuberculosis patients mainly from West Newland, but also from the whole south coast of Finland. It was established in the 1950s. As the number of tuberculosis patients diminished, the hospital was reorganised to serve patients in the specialties of internal medicine and pulmonary diseases. The hospital then also needed laboratory services for clinical physiology. In 1983, associate professor Antti Viljanen was nominated as the chief physician of clinical physiology, and he made a big effort to build up the laboratory according to the Swedish model with good selection of traditional cardiorespiratory measurements and nuclear medicine imaging with a gamma camera.

A good selection of lung function studies, long-term ECG recordings and echocardiographic imaging were included. For administrative reasons Meltola Hospital was closed in 1996, and part of the laboratory equipment was installed in Jorvi hospital. The last chief physician in clinical physiology at Meltola Hospital was Jarl-Erik Nyman.

The predecessors of the **South Karelia Central Hospital** that operates in Lappeenranta are Tiuruniemi Tuberculosis Sanatorium, Viipuri Provincial Hospital, which was ceded to the Soviet Union after the World War II, and Southern Saimaa Central Hospital. Tiuruniemi Hospital was closed in 1992. Since 2010, the central hospital has been part of South Karelia's District of Social and Health Care (Eksote).

The clinical physiology and nuclear medicine unit was established in the hospital in 1993, when the hospital's allergy and lung function laboratory and nuclear medicine laboratory were combined. Since then, the unit has been equipped with modern research equipment and more than 7000 studies are carried out there each year. The permanent staff consisted of a senior physicist, Kari Tahvanainen, and nine members of the care staff. Medical expertise has been gained from outside the hospital.

Päijät-Häme Central Hospital in Lahti was established in 1976. Specialist physicians in clinical fields carried out clinical physiology studies for a long time. Nuclear medicine studies were carried out for a long time in the clinical chemistry laboratory, and the senior physician had a long career in the field of nuclear medicine studies. The first physician position in clinical physiology was established at the hospital in 2005, when associate professor Tuomo Lantto became the senior physician. The first senior physicist, Matti Karhunen, retired in 2010, and he was succeeded by senior physicist Antti Sohlberg. The senior physician of the unit has been Hannu Koivu since 2014. The staff of the unit consists of a senior physician, a senior physicist and nine members of care staff.

4 | DEVELOPMENT OF CLINICAL PHYSIOLOGY IN THE TAMPERE UNIVERSITY HOSPITAL AND SURROUNDING REGIONS

4.1 | Clinical Physiology in Tampere University Hospital

4.1.1 | Between 1960 and 1980

Pulmonary and respiratory research in the area of clinical physiology was carried out by interested physicians until the end of the 1960s in clinics specialising in respiratory medicine, internal medicine, paediatric medicine and surgery. This changed at the end of the 1960s when the management of the hospital decided to establish a clinical physiology laboratory in the hospital in accordance with the Swedish model. Arto Uusitalo, who had graduated in Helsinki and had gone to the Uppsala academic hospital in 1965 to study the subject and familiarise himself with the laboratory organisation, was given to the responsibility to establish the laboratory.

After his 2-year-long training period, Arto Uusitalo was appointed as the senior physician of the new laboratory that had been founded in 1967. The operating plan from 1967 for the clinical physiology laboratory for the years 1968–1970, which was prepared

by senior physician Uusitalo, states that 'Operations are planned in accordance with generally prevailing principles in Scandinavia, whereby the laboratory shall carry out patients' diagnostic and treatment-related studies using the most diverse clinical physiological study methods and in close collaboration with the treatment units and other laboratory units in accordance with the needs present at the hospital. … The operations of the laboratory shall be started based on the clinical physiology-related (ECG, PAV, etc.) studies of the current cardiorespiratory research department and currently subordinated by the central laboratory, and the operations shall be expanded in accordance with the previously mentioned principles. On one hand, laboratory studies are divided into tests which are carried out in the laboratory in accordance with the attending physician's referral; on the other hand, special studies that are carried out in direct collaboration with the attending physician and in which the laboratory provides technical and methodical assistance (e.g., cardiac catheterisations).'

The first clinical exercise tolerance test in accordance with the new model was carried out on 22 November 1967. The laboratory was quickly equipped with modern testing equipment, complete with invasive and noninvasive examination equipment for the cardiovascular and pulmonary system and a separate catheterisation room. Gastrointestinal physiology tests included pressure measuring equipment, intestinal biopsies testing for pancreatic and ventricular special functions. The unit also carried out all the hospital's blood gas analyses, which were the responsibility of the unit's own chemist. The personnel, which the new senior physician trained, was initially obtained from the other units of the hospital. Both of the hospital's cardiologists, Eila Leskinen and Marianne Viitanen, also operated in the established unit.

The nuclear medicine laboratory, which was initially established in the radiology unit, was moved to the clinical physiology unit in 1971 and placed under the management of senior physician Lauri Pöyhönen and senior physicist Erkki Vauramo. The unit's initial testing equipment included a Nuclear Chicago gamma camera and nephrography equipment as well as individual probes for the analysis of samples.

The clinical physiology laboratory quickly gained an important position in the hospital by serving the clinical units with its tests and scientific research that met international quality requirements. The unit had a service point at the hospital for pulmonary diseases in Pikonlinna, where a modern lung function laboratory was established by the aid of associate professor Anssi Sovijärvi. In addition to ordinary dynamic spirometry computerised flow-volume recordings were started. The laboratory could also measure pulmonary diffusing capacity, lung volumes with the gas dilution method, pulmonary mechanics and lung volumes with body plethysmography, distribution of pulmonary perfusion, ventilation and lung volumes with Xe-133-multidetector radiospirometry (Valmet Bi-1200), exercise capacity with treadmill and bicycle devices and BHR test with inhaled methacholine. Reference values for radiospirometry were published.

4.1.2 | Between 1980 and 2000

During this time period, a rapid digitalisation of all testing equipment took place. The special domain of the clinical physiology unit became daily ambulatory registrations such as ECG, blood pressure and oesophageal pH monitoring and manometry. The nuclear medicine laboratory was equipped with modern cameras, GE's Radi and Maxi cameras, which could also be used to carry out tomography scans. The nuclear medicine laboratory's physicist Antti Virjo was also an important developer of the gamma-11 system.

The unit moved to new premises in the late 1980s, and these premises were designed based on functional requirements. At the same time, clinical physiology and nuclear medicine moved into shared premises. In the 1990s, the number of tests was high. The number of resting ECGs was approximately 50,000/year, and the number of blood gas analyses and exercise tolerance tests was in total almost 2000/year. Blood gas and ECG registrations were later transferred as bulk deliveries to the laboratory center.

In 1984, senior physician Arto Uusitalo (Figure 7) was appointed as Finland's first professor of clinical physiology at the University of Tampere's Faculty of Medicine. Arto Uusitalo operated as senior physician, for almost 30 years until 1995, when he became the entire hospital's and hospital district's medical director. With a wide network and as an excellent negotiator, Professor Uusitalo built and developed the laboratory, based on what he had learned from Sweden, into a research laboratory that met international standards. Väinö Turjanmaa became his successor as senior physician (Figure 7).

4.1.3 | Between 2000 and 2020

At the turn of the millennium, the organisational model of the hospital changed in a radical manner. The old clinic-led administrative model was abandoned and replaced with divisions. Clinical physiology and nuclear medicine were included in the same division as radiology, neurophysiology and the hospital pharmacy. In 2002, the hospital administration decided to make the division a public utility. The new conglomerate was established in 2004, and it consisted of clinical physiology, clinical neurophysiology and radiology, with all the hospital physicists in their own division. The senior physician in clinical physiology, Väinö Turjanmaa, who had operated as the leader of the 2-year development project, was appointed as the first managing director. He was given the title of professor in 2000, after Arto Uusitalo.

Today, the unit has modern equipment for both clinical physiology and nuclear medicine. The personnel of the unit includes a senior physician, eight specialists, four residents and two physicists. Furthermore, the unit has a care staff with 29 members of and five assisting staff members. About 17,000 examinations are annually carried out at the unit, including more than 5000 examinations in nuclear medicine.



FIGURE 7 Professors of Clinical Physiology at the University of Tampere. Arto Uusitalo (right) 1984–1998, Väinö Turjanmaa (left) 2000–2006 and Mika Kähönen (middle) 2006

4.1.4 | Activities in research and development in Tampere

Since the beginning, the unit has participated in a number of scientific projects carried out at the hospital. The first theses were published in the late 1970s: Lauri Pöyhönen's *Partial nephrographies in the screening of renal diseases in hypertensive patients* in 1976 and Asko Seppänen's *Cigarette smoking, carbon monoxide pollution and their effects on physical and neurobehavioral performance* in 1977. Today, several thesis projects are underway each year under the guidance of professor, senior physician Mika Kähönen (Figure 7). He was granted the title of professor in 2006.

Much development work on methods has been carried out in the unit at the lead of professor Uusitalo. The 16 radiospirometry detectors of the multiprobe system were introduced already in the late 1970s. In 1981, in collaboration with VTT/SAI (professor Niilo Saranummi and professor Antti-Pekka Ahonen), the technique of invasive ambulatory blood pressure measurement developed at London's Clinical Research Centre was introduced. An entirely new computer-based analysis method was developed for it with an Apple II computer. This method was used with the Karolinska Institute (professor Mats Fredrikson and psychologist Martti Tuomisto) to determine the reactive effect caused by ambulatory measurements as a cause of hypertension. This study is ongoing. In the 2000s, a wide-scale study on cardiovascular diseases with more than 4000 people concerning was carried out to collect data for the Finnish Cardiovascular Study (FINCAVAS). Routine clinical exercise tolerance tests were carried out for the study in willing participants at the clinical physiology laboratory.

The CircMon device, which is based on whole-body impedance measurements, was developed by specialist and later senior physician Tiit Kööbi in collaboration with Estonian engineer Jürgen Lamp. The device is in everyday use both for daily routine purposes and scientific purposes to register hemodynamic variables.

The unit is participating in several wide-scale Finnish and international research projects at the lead of current professor Mika Kähönen.

4.2 | Clinical physiology in other hospitals surrounding Tampere

An independent clinical physiology unit was established at the **Seinäjoki Central Hospital** in the early 1990s, and its first senior physician was Pertti Oinonen. Clinical physiology studies, such as clinical exercise tolerance tests, spirometry, ultrasound scans and nuclear medicine studies, had been carried out at the hospital since the 1970s in the clinical chemistry unit. Physicians of other fields of specialisation were responsible for these studies. Since its establishment, physicist Martti Männikkö served as the senior physicist of the unit for several years. There have been several physicians at the unit after Pertti Oinonen. Specialist Esa Kauppila is currently responsible for operations, while Jussi Haanpää operates as the senior physicist. In terms of administration, the unit is nowadays located in the radiology unit.

The premises of **Kanta-Häme Central Hospital's** clinical physiology unit, which is located in Hämeenlinna, were modernised in 1979. Nuclear medicine studies were also carried out in the clinical physiology unit. The physicians Arto Uusitalo and Lauri Pöyhönen from Tampere Central Hospital's clinical physiology unit played a significant role in the design of the unit. The first senior physician at the clinical physiology unit was physician Pekka Halttunen, who served in the role since 1980. In the early stages, TAYS physicists Antti Virjo and Matti Koskinen operated as physicists, until Keijo Saali was appointed to the newly established position of senior physicist in which position he continues to operate today. Since 1982, the senior physician of the unit was a specialist in clinical physiology, Lauri Karhumäki, who held the position for almost 20 years. During that

time, the unit was developed significantly in terms of both studies and staff. The clinical physiology unit of Kanta-Häme Central Hospital has also been administratively moved to the radiology unit, but its operations are managed by the physician and senior physicist of the field.

5 | DEVELOPMENT OF CLINICAL PHYSIOLOGY IN THE TURKU UNIVERSITY HOSPITAL AND SURROUNDING REGIONS

Turku University Hospital is a continuation of the first hospital in Finland, established by the King of Sweden Adolf Fredrik in 1756. After losing a war against Russia, Sweden had to cede Finland to the Czar of Russia in 1809. A teaching hospital related to the Academy of Turku (established in 1640) was built in 1827. Only 2 weeks after the building was ready, a fire devastated the city. After the fire, the Academy was moved to Helsinki. The hospital building was not used as a hospital and later accommodated Russian soldiers.

Turku University was established in 1920, but without a medical faculty. The communities in the Turku area and the state of Finland together built a new hospital in 1938. It was the first central hospital in Finland. It became a university hospital in 1943, when the second Finnish medical faculty was established at the University of Turku during the World War II. At the beginning, there were no preclinical departments—the students studied their first years in Helsinki and continued their clinical studies in Turku. The theoretical institutes were built in 1954 next to the university hospital, when preclinical studies began in Turku.

5.1 | Clinical physiology and nuclear medicine in Turku have their roots in the departments of physiology and pharmacology

Professor Kaarlo Hartiala was the first professor of physiology in Turku. He, together with several clinicians from the hospital, established the Cardiorespiratory Research Unit in the Department of Physiology in 1956, with the goal to achieve an international level in cardiac diagnostics and treatment. They managed to get private funding for the necessary equipment.

Tuomas Peltonen (later professor of paediatrics), Heikki Kalliola from the department of internal medicine and Sakari Einola from the surgery department practised cardiac catheterisation in Stockholm in 1956. Thereafter both adult and paediatric cardiac catheterisations were performed in this unit until 1970, when this activity was moved to the hospital departments of clinical physiology, radiology and paediatrics. Sauli Viikari (later professor of surgery) performed the first open-heart surgery in Finland in this unit in 1960. When open-heart surgery continued later in the hospital Department of Surgery, thoracic surgeons practised with animals in the unit. Today its main focus is on epidemiology of the risk factors of atherosclerosis (The Young Finns Study).

In 1957, Kaarlo Hartiala also established the Sports Research Unit in the Department of Physiology. It developed methods of exercise testing and also provided sports medical consultations. The unit is now called Paavo Nurmi Center, and it mainly focuses on the health consequences of physical activity and inactivity.

At the end of the 1950s, Panu Vilkki (later chief of paediatric surgery) started nuclear medicine studies in the Department of Pharmacology by studying thyroid function with radiolabeled iodine. Nuclear medical studies were moved to the hospital department of radiation therapy already in 1960. In 1987, the department of nuclear medicine was established in the university hospital as the first independent nuclear medicine department in Finland.

The Turku Medical Cyclotron project was started at the end of the 1970s as a multidisciplinary project between Turku University, Åbo Akademi and Turku University Hospital. From a modest start, it has developed to the National PET Center with over 200 research workers.

After several organisational changes and the formation of the combined specialty of clinical physiology and nuclear medicine the hospital now has the Department of Clinical Physiology, Nuclear Medicine and PET Studies.

Clinical physiology was introduced to the basic medical education already in the early 1970s, but it took about two decades before it (later clinical physiology and nuclear medicine) was recognised as an independent discipline of the medical faculty. The first professorship in the field was established in 2003.

5.2 | Clinical physiology in Turku University Hospital

Turku University Hospital opened a new building in 1968. Then, with strong support of professor of paediatrics Tuomas Peltonen and chief of the Central Laboratory associate professor Bernt Laurent, the hospital also started a clinical physiology laboratory. Heikki Wendelin was recruited as its first physician. His position was in the Central Laboratory, whereas all other personnel belonged to the Department of Paediatrics, and the laboratory was located inside the facilities of the department of radiology!

Heikki Wendelin had worked in the Cardiorespiratory Research Unit since 1966 and continued specialisation in the hospital until 1972, when he was granted the specialty of clinical physiology. He also had his doctoral dissertation in 1972 and became an associate professor in 1973. He was nominated the first chief physician of the department in 1976 (Figure 8). Naturally, the selection of studies was first rather limited, but grew rapidly. It is worth mentioning that the laboratory was among the first in the world to start Holter recordings.

Cardiac catheterisations were started in the hospital in 1970 in collaboration with cardiologists, radiologists and paediatric cardiologists. Heikki Wendelin trained all residents to perform right side cardiac catheterisations. He also started together with cardiologist Matti Arstila cardiac thallium scintigraphy already in 1978 in the Department of Radiotherapy as the first laboratory in



FIGURE 8 Associate professor Heikki Wendelin



FIGURE 9 Professor Jaakko Hartiala

Finland. Also, cardiac ultrasound studies started already in the late 1970s.

After coronary bypass surgery was started in Turku, the increasing demand for clinical physiology studies necessitated extension of the facilities. Heikki Wendelin carefully studied clinical physiology laboratories in Sweden. That resulted in a multidisciplinary new laboratory in 1981 established in the old hospital. There clinical physiology, angiocardiology and nuclear medicine laboratories worked in close proximity and their physicians, physicists and other personnel collaborated without organisational boundaries. In 1982, the first coronary angioplasty in Finland was performed there.

The purchase of a Marquette data ECG system already in 1983 was a far-sighted achievement. The service has later grown to a regional ECG service now with well over 2.2 million resting ECG's and additional exercise ECG's and Holter recordings.

Heikki Wendelin was also the chairman of the Turku Medical Cyclotron Project, and made preparations to start PET studies in Turku. For that purpose, a 700 m long pipeline from the cyclotron in Åbo Akademi was built to the new laboratory to deliver short-lived oxygen-15 isotope to the dual-head ROTA-gamma camera.

Heikki Wendelin had laid a sound basis for the functioning of a modern and well-equipped laboratory, when he died at the age of 42 years in 1984. He was succeeded by Jaakko Hartiala, who had just 6 months earlier returned from a 2-year postdoctoral period from the University of California San Francisco (UCSF) where he made experimental asthma research. Chief of the angiocardiology department Uno Wegelius succeeded Heikki Wendelin as chairman of the Turku Medical Cyclotron Project. Jaakko Hartiala was nominated as a half-time professor of clinical physiology and nuclear medicine in 2003 (Figure 9).

The growing coronary bypass activity yielded three new consultants, one physicist and six laboratory nurses plus two other persons so, that at 1988 the total number of staff was already 26 persons. The new consultants were Markku Saraste 1983, Eino Hietanen 1985 and Kari Antila 1989. They all had been researchers in the Department of Physiology, and Hietanen and Antila had spent postdoctoral periods in New Jersey and in Halifax. They had different interests in medicine: Saraste echocardiography, Hietanen gastroenterological studies and Antila both the autonomous nervous system and data ECG.

The hospital purchased the first colour Doppler ultrasound machine in the Nordic Countries in 1985. This started Markku Saraste's a long period of methodological development and educational activity. Echocardiography became the new 'flagship' of the laboratory and largely replaced the need of cardiac catheterisations.

Eino Hietanen started new gastrointestinal studies, and Kari Antila was responsible for the medical development of data ECG. Unfortunately, Hietanen died already in 2002, and Antila moved on to private medicine in 2001.

Jaakko Hartiala was a visiting associate professor in 1991–1992 at the Department of Radiology at UCSF, where he studied functional MRI of the heart. He started this activity in Finland in collaboration with local radiologists and continued MRI research in Turku with his collaborator at UCSF, professor Hajime Sakuma from Mie University, Japan.

Olli Raitakari started as a consultant in 1996. He had a 2-year postdoctoral period studying mechanisms of atherosclerosis in Sydney and returned to Turku in 1999. He became chief of the clinical physiology laboratory in 2004. Later in 2007, he was nominated part-time professor cardiovascular research in Turku

University and the chief of the Cardiorespiratory Research Unit, which was changed to full-time professorship in 2016 (Figure 10).

Maria Saarenhovi (daughter of Heikki Wendelin) was nominated chief of the clinical physiology laboratory in 2016. After Jaakko Hartiala retired in 2016, chief of the PET Center professor Juhani Knuuti was appointed as the chief of the Department of Clinical Physiology, Nuclear Medicine and PET Studies (Figure 11) and Jukka Kemppainen as a full-time professor of clinical functional imaging in 2019 (Figure 12).

5.3 | Lung function tests, Paimio Hospital

The Department of lung diseases was located in Paimio Hospital designed by famous architect Alvar Aalto. As the hospital was 30 km from Turku, the demand of pulmonary function tests in Turku University hospital was rather limited although the clinical physiology laboratory had a full pulmonary function laboratory, including body plethysmograph and later also radiospirometry.

Ritva Tammivaara became a specialist in clinical physiology in 1971 and did her doctoral dissertation in Uppsala Akademiska Sjukhuset in Sweden. She returned to Finland in 1973 and started specialisation in lung diseases in Paimio Hospital. She extended the clinical physiology studies in Paimio from volumetric spirometry and cycle exercise testing to flow-volume spirometry (also in obstruction provocation tests), nitrogen wash-out studies, treadmill exercise tests, blood gas analysis during exercise and hyperventilation and sleep recordings.

A comprehensive clinical physiology laboratory was built in Paimio Hospital in 1987, when it was united with Turku University Hospital. At this point also radiospirometry was moved from Turku to Paimio and clinical physiologists from Turku performed studies there. Later gamma camera studies in Turku replaced radiospirometry in lung ventilation/perfusion studies, and this laboratory was closed.

In 2003, a 'virtual' allergology unit was founded in a new hospital building in Turku. The Department of Clinical Physiology moved its pulmonary function laboratory there. Later the Department of Lung Diseases also moved to this new building, and the number of pulmonary function studies soared. In 2013, the whole clinical physiology laboratory moved to the new hospital building.

5.4 | Nuclear Medicine in Turku University Hospital

Nuclear medicine was established in Turku University Hospital in 1960 by Bengt Laurent, chief of the central laboratory. He had studied nuclear techniques both in Sweden and in England, and performed thyroid scans. At that time the tests were made in the



FIGURE 10 Professor Olli Raitakari



FIGURE 11 Professor Juhani Knuuti



FIGURE 12 Professor Jukka Kemppainen

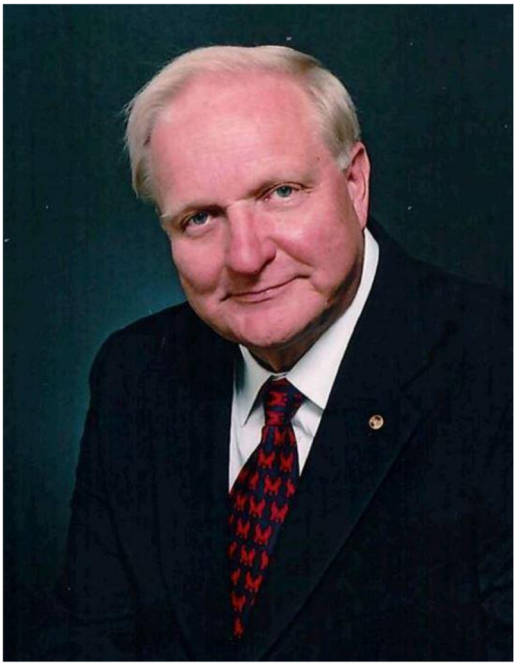


FIGURE 13 Associate professor Risto Härkönen

department of radiation therapy mainly to detect brain tumours and metastases. In 1968, a Finnish-made (Wallac) renograph and the first gamma camera (Phogamma-3) were installed.

In 1981, a dual-head Rota-camera was installed in the Laboratory of Clinical Physiology to make SPECT scans of the myocardial perfusion with ^{201}thallium and pulmonary ventilation/perfusion scans with ^{81m}krypton/^{99m}technetium. It was also tested in imaging myocardial perfusion with $^{15}O_2$ before the first PET camera was installed in 1988. The ^{81m}krypton gas was eluted from a generator produced in the cyclotron at Åbo Akademi, and the ^{15}O was transferred via a 700 m long pipeline from the cyclotron to the hospital.

The Department of Nuclear Medicine was formed in 1987. Risto Härkönen started as the chief of the department in 1989 (Figure 13). At that time the staff consisted of five physicians, three physicists, one radiochemist, one hospital engineer, 11 technicians and two secretaries. There were four gamma cameras, and also the new PET camera belonged to this department before the PET Center was established in a separate building in 1999. The number of different nuclear tests was over 40, the most common of which were bone scans and myocardial perfusion studies.

In the mid-1990s, after the formation of the combined specialty of clinical physiology and nuclear medicine, the organisations were also combined. After Risto Härkönen retired, Marko Seppänen was selected chief of the nuclear medicine laboratory in 2008. With the development of hybrid imaging, the first SPECT-CT was installed in 2005, and currently the laboratory has three SPECT-CT scanners. The latest, a 16-row scanner, was installed in 2017.

5.5 | From the Turku Medical Cyclotron project to The National PET Center

The professor of physics at Åbo Akademi, Mårten Brenner, was the former chief physicist of the Department of Radiation Therapy in Helsinki University Hospital. Already since the mid-1960s, he worked hard to get a cyclotron to Åbo Akademi for basic physics studies and also for proton therapy. After several attempts he, together with another physicist, Erkki Vauramo, succeeded in their pursuit, and the cyclotron was bought from the Soviet Union to balance the bilateral trade deficit. It was installed in 1974.

A committee, formed in 1976 by the Ministry of Education, made plans of an Institute of the Medical Use of Nuclear Radiation in Turku. As there were no direct clinical applications at that time, Turku University Hospital was originally rather critical of the plan, but the medical faculty set up a project group to further develop the idea. Heikki Wendelin was chosen as the chairman of the group, which made a detailed plan to the faculty in March 1977. Already in October 1977 'Symposium on the Medical Application of Cyclotrons' attracted almost 100 attendants to Turku, among them many international experts in this new field. It became clear that at that point it was fundamental to concentrate on basic research, and that potential clinical applications should wait.

The University of Turku established a radiochemistry laboratory close to the cyclotron, as the production of nuclear probes was essential for the development. The laboratory first produced ^{81}Rb-^{81m}Kr-generators and ^{123}Iodine. The krypton generators were delivered to several hospitals in Finland in cooperation with the Finnish Air Force and even to Copenhagen and to Oslo. Later the laboratory in collaboration with international experts produced

also ^{67}Ga, ^{111}In, ^{123}I, ^{52}Fe and ^{201}Tl for gamma camera studies. The first positron emitters were ^{11}C and ^{15}O isotopes and later ^{18}F-radioisotypes, especially ^{18}F-FDG first in Europe. It was used in animal studies but was also delivered to Karolinska Institute in Stockholm for patient studies.

Heikki Wendelin died in 1984, and radiologist Uno Wegelius continued as the chairman of the project. The project had made a 3-year research contract with the Academy of Finland in 1982. Wegelius managed to get a 3-year extension of this funding in 1985. He also got the Ministry of Education, University of Turku and Turku University Hospital to buy the first PET camera, which was installed in 1988. Turku University Hospital, Turku University and Åbo Akademi made an agreement to jointly develop PET research in Turku—this agreement is still unchanged!

The first PET camera opened door to human PET-studies. In the first year, their number was only 83, but the use of PET gradually increased in various fields of research: neurology, cardiology, hepatology, oncology, paediatrics and psychiatry. Unlike many other centers, all studies were quantitative, which necessitated measurement of the radioactivity concentration of blood samples. The production of ^{15}oxygen greatly enhanced the selection of studies. This yielded increasing number of research papers and made possible research funding from pharmaceutical companies.

In 1996, the Ministry of Education nominated the unit as National PET Center and also granted new resources, among them the second PET camera. At the same time, Turku University Hospital agreed to build a separate large building for the PET Center. At this point, when the unit was on a secured basis, Uno Wegelius retired and was succeeded by Juhani Knuuti, who had completed his doctoral thesis there a few years earlier.

The planning of the new building was a vast task, in which especially physicist Mika Teräs was heavily involved. The building was ready in 1999. The number of research groups increased rapidly and also three research professors, Pirjo Nuutila (metabolic research), Juha Rinne (brain mediator research) and Harry Scheinin (drug development) were recruited and three other researcher positions were established. Also, a third PET camera was purchased.

The growing activity also necessitated new funding, which was provided with a long research agreement with Amersham Ltd in 2003. It was one of the biggest in the history of Finnish academics and made possible to purchase the fourth PET-camera, and a 1.5 T MRI-scanner. The agreement consisted also a professorship of radiochemistry in Turku University and equipment for radiochemistry. Olof Solin was invited to the new post. Education in radiochemistry started at the University of Turku, and radioligand production was developed to comply with the quality standards of the pharmaceutical industry.

At the time of the collapse of the Soviet Union, it owed Finland 670 million euros. Russia promised to take care of it. Åbo Akademi got another cyclotron worth 3 million euros in this debt conversion arrangement. It was installed in the PET Center and was operational in 2007.

In 2005, the first PET camera was replaced after 17 years and 11,000 studies with a PET/CT-camera, which made possible also coronary CT in conjunction to ^{15}O cardiac studies. In 2006, an animal PET/CT was also purchased to increase preclinical studies. In 2010, the first PET/MRI-camera was purchased, and in 2019 it was replaced with an integrated PET/MRI-scanner and in 2021 one of the first total-body PET/CT cameras in the world was ordered. The radiochemistry production has greatly increased and complies with GMP standards.

The Academy of Finland nominated the 'Research group of molecular imaging in vascular and metabolic research' as a Center of Excellence for 2008–2013 and later renewed the status for another 6 years.

Today the PET Center consists of almost 200 persons. It produces annually about 6.000 imaging studies. At the end of 2021, it has produced over 170 academic dissertations, over 2800 original publications and is the most prominent research unit of Turku University.

5.6 | Clinical physiology in other hospitals surrounding Turku

In **Pori Central Hospital**, clinical physiology studies were originally performed in the central laboratory. Internists supervised exercise tests in the laboratory, but other tests were performed mainly by laboratory nurses, one of whom also performed echocardiography. The first specialist in the field, Risto Härkönen, worked in Pori between 1977 and 1978. The first physicist Olli Tannila started in 1978, when the first gamma camera was installed. After his retirement, he was followed by Virpi Tunninen in 1998.

The first chief physician was Pekka Varjo, who was in charge of the department from 1986 until his retirement in 2018. During this time, the department increased the selection of tests to Holter recordings, colour Doppler echocardiography, esophageal manometry and pH recording, regional data ECG system, myocardial scintigraphy, later SPET-CT and finally in 2018 PET-CT.

The hospital also established another specialist position, but it has been occupied only for short periods. Therefore, already in Pekka Varjo´s time telemedicine played a substantial role especially in nuclear medicine studies by specialists in Tampere University Hospital. After his retirement, both nuclear medicine and also suitable clinical physiology studies have been analysed by specialists in Turku University Hospital. Just recently, Petri Kallio has started as a chief physician in 2021.

At the moment the staff consists of 21 persons: two specialists (both vacant), two physicists, eight laboratory and three radiology nurses together with four other nurses and two secretaries.

In **Vaasa Central Hospital**, the first chief physician in the Department of Clinical Physiology was Olli Wanne, who worked in the department between 1985 and 1990, when he started as the chief physician in the Department of Paediatrics as he had completed training in both specialties. During his time, the department

performed for example, exercise tests, pulmonary function tests, echocardiography and a variety of nuclear medicine tests, which were earlier performed in the chemistry laboratory.

Risto Niemi succeeded Wanne in 1990. His main interest was in cardiac studies, and during his 30-year period in Vaasa he also specialised in cardiology. Besides echocardiography and myocardial scintigraphy, he started cardiac MRI in Vaasa. Actually, the nuclear medicine department had long been a separate unit, but Niemi also worked there. During his last years, the hospital had also one resident from Turku University hospital for 2 years, which Risto Niemi appreciated greatly.

Due to a lack of other specialists, already in Risto Niemi´s time telemedicine played a substantial role, especially in nuclear medicine studies, which were interpreted by specialists in Tampere University Hospital. After his retirement, both nuclear medicine and suitable clinical physiology studies have been analysed by specialists in Turku University Hospital.

5.7 | Clinical physiology outside hospitals in Turku

5.7.1 | Cardiorespiratory Research Unit in Turku University

The unit was established in 1956—12 years before the first hospital laboratories of clinical physiology in Finland. Its main motive was to achieve an international level in modern cardiac diagnostics and treatment. It was at the beginning an informal joint venture of basic physiologists and clinicians, located in the Department of Physiology. The department head was professor Kaarlo Hartiala, who was a specialist in internal medicine. During his Rockefeller fellowship in 1948–1950 in the University of Chicago, he also became motivated to develop clinical physiology in Finland.

At first, Hartiala worked there together with the professor of radiology Carl Wegelius, associate professor of medicine Eino Linko, Tomi Peltonen (later professor of paediatrics and chief of the Cardiorespiratory Research Unit) and Sauli Viikari (later professor of surgery). Before starting cardiac catheterisations, Peltonen together with internist Heikki Kalliola and surgeon Sakari Einola studied catheterisation techniques in Karolinska Insitutet in Stockholm. The Finnish Ministry of Education provided funds to buy the radiology equipment. After this, all cardiac catheterisations in Turku were performed in the Cardiorespiratory Research Unit for over 10 years.

The ultimate goal was to perform open-heart operations in Turku. The modern heart-lung machine, funded mostly privately, was installed in 1958. It was first used to practice the operations with dogs. Thereafter, the first open-heart operation in Finland was performed there by Sauli Viikari in April 1960.

Another research line was experimental studies with sheep and pigs to study the adaptation of circulation at birth and the physiology of the first breath. Later, after invasive patient studies and cardiac surgery were moved to the hospital, experimental studies continued in the unit. Timo Savunen (later the chief of the Department of Surgery) and his group studied the mechanisms, prevention and treatment of ischaemic perfusion myocardial injury in open-heart surgery with pigs. Moreover, Pekka Kääpä (later professor of medical education) studied for example, the effects of meconium aspiration in pigs.

One interest in the early years was to study the exceptional maximal oxygen uptake in elite athletes, was it mainly genetic or due to training? To this aim, some Olympic runners volunteered in exercise testing experiments. Later, associate professor of cardiology Matti Arstila developed pulse conducted exercise test methodology and also collected normal values of exercise capacity of the Finnish adult population.

Tuomas Peltonen was an active aircraft pilot, and he started the mandatory medical testing of permit to fly for private pilots in the unit. This activity continued for three decades.

Already in the 1970s, associate professor Kari Antila developed computerised analysis methods of ECG, which were widely used for example, to monitor newborn babies in intensive care, especially the heart rate variability. He and earlier associate professor of paediatrics Ilkka Välimäki had spent postdoctoral periods in Dalhousie University (Nova Scotia, Canada) in professor Pentti Rautaharju´s laboratory to study these techniques.

In the late seventies, a multicenter study to explore the risk factors of atherosclerosis in children and young adults (The Young Finns Study) was started in Finland. In the first data collection in 1980, 3596 young persons aged from 3 to 18 years from different areas in Finland participated. Jorma Viikari from the Cardiorespiratory Research Unit (later professor of internal medicine) was one of the pioneers organising the study. Later, the office of this still after 40 years ongoing study was moved from Oulu to Turku, and clinical physiologist Olli Raitakari, chief of the Cardiorespiratory Research Unit since 2007 and professor of cardiac research) became the chief of the Young Finns Study. He organised the data collections in 2001, 2007, 2011 and 2018–2020. The most recent phase of the study is epigenetic research to explore the role of the health behaviour of parents and grandparents in the health of their offspring. The study is currently the largest in Europe and most thoroughly characterised follow-up study from childhood to adulthood in the world, now funded also by the European Research Fund. It is also a part of a N.I.H. -funded i3C consortion together with similar studies in the USA and Australia.

Another population study in the Cardiorespiratory Research Unit is an intervention study to prevent atherosclerosis (The Strip Project). It was started in 1990 by Olli Simell (professor of paediatrics). It is the largest and longest dietary intervention project in the world consisting of 1062 toddlers aged 7 months at the onset of the intervention. The children were randomised into intervention and control groups. The families in the intervention group got dietary and health counselling until the children became 20 years old.

The results of both the Young Finns Study and the STRIP Project have strongly influenced both Finnish and international (e.g., the American Paediatric Society) dietary and health recommendations.

5.7.2 | The Paavo Nurmi Center in University of Turku

Professor Kaarlo Hartiala established the Sport Medical Research Unit (later named Paavo Nurmi Center) in the Department of Physiology in 1957. It is one of the six sports medical centers in Finland, and the only one as part of the university. It is located in close proximity to the Cardiorespiratory Research Unit, and has collaborated closely with it. Kaarlo Hartiala was the chief medical officer of the Finnish team in several Olympic games. The research with elite athletes explored at his time the influence of blood haemoglobin composition and the effect of high altitude on the exercise capacity. The latter was especially relevant before the Olympic Games in Mexico City in 1968.

Later, when Olli Heinonen (professor of healthy exercise) became the chief of the unit, its focus has widened to the influence of physical activity and inactivity on the health of the population. Besides research and education in the field, it performs exercise testing of healthy persons and advocates the benefits of physical activity to the public.

The hospital Department of Clinical Physiology has served as one of the clinical training sites for physicians specialising in sports medicine. This has led to closer collaboration in sports medicine and has also facilitated special diagnostics and treatment paths for sports medical patients in the hospital.

5.7.3 | The Rehabilitation Research Center of The National Social Insurance Institution in Turku

This center to study and develop rehabilitation methods for several patient groups was established by the National Social Insurance Institution in 1970. After the new facilities were built, it started operation in 1972. Its first chief was cardiologist Veikko Kallio (later professor of rehabilitation). As coronary heart disease was the leading cause of death of work-aged men in Finland, the development of rehabilitation after myocardial infarction was one of the major tasks of the center.

For this aim, the center built a comprehensive laboratory of clinical physiology. Its first chief of clinical physiology was Ilkka Vuori, whose background was in the Sports Medical Research Unit. He later spent a postdoctoral period in Stanford University. The laboratory´s activity widened from exercise testing, Holter recording, spirometry and 24-h blood pressure to spiroergometry, echocardiography and nuclear methods to study skeletal muscle blood perfusion and later for example, to autonomic nervous function tests and carotid sonography.

The center supported strongly the Finnish Society of Clinical Physiology in its education activities. Several methodological symposia of the field were arranged in the early years on its premises, and several publications of the symposia were printed in its publication series in addition to the research papers produced there. One of the main research achievements of the center in rehabilitation area was to show that early physical activity after myocardial infarction is superior to bed rest. This philosophy rapidly was adopted in patient care. In 2004, the laboratories of the center were united with the Finnish Institute of Health and Welfare in Helsinki, and its laboratories in Turku were later closed.

5.7.4 | Private clinical physiology activity in Turku

Turku has traditionally had a strong private medical field, originally divided into several different private companies. In the last two decades, most of them have been consolidated to two nationwide chains.

The first private clinical physiology laboratory in Turku was established by Heikki Wendelin, Ilkka Vuori and Matti Arstila in 1972 in Laboratory Vuori, one of the oldest private medical companies in Finland. At the same time, Heikki Wendelin started another laboratory in a newer private medical center Vagus. These laboratories performed mainly exercise testing and Holter recordings, the number of exercise tests equalling to the public sector. Heikki Wendelin died in 1984, and thereafter Matti Arstila, Jaakko Hartiala and Markku Saraste started a new company, Turku Heart Center, in another private medical center, Turun Lääkärikeskus (later Meditori). There echocardiography became one of the main activities.

In 1992, another private clinical physiology laboratory headed by Eino Hietanen was started in a newer and large private medical company called Pulssi. It performed tests similar to the two others, but Pulssi also had a pulmonary function laboratory. In 1996 Meditori and Vagus merged together, and in 2001 the new company became part of the first nationwide chain Mehiläinen. In this process, their clinical physiology laboratories were united in Mehiläinen.

In 2008, Suomen Terveystalo, another nationwide private medical chain, also established a clinical physiology laboratory headed by Markku Saraste and Jukka Kemppainen in their new medical center in Turku. Three years later Suomen Terveystalo bought Pulssi, and again the two clinical physiology laboratories were united in Pulssi.

There is also one telemedical company based in Turku, iRad Molecular Imaging, headed by Jukka Kemppainen. It was established in 2013. It operates nationwide in the field of clinical physiology and nuclear medicine and offers its services to public laboratories lacking specialists in the field. It has consultants working in several cities in Finland.

6 | DEVELOPMENT OF CLINICAL PHYSIOLOGY IN KUOPIO UNIVERSITY HOSPITAL AND SURROUNDING REGIONS

6.1 | Early stages at Kuopio Central Hospital and Tarina Sanatorium

Kuopio Central Hospital was established in January 1959 in the new Puijo Hospital. In addition to the ECG, the methods used were the

recordings of pulse curves and phono-, vector- and ballistocardiographies. Clinical exercise tests were included in practice in the early 1960s. During this time, patients with pulmonary diseases were treated in the Tarina Sanatorium, where the most common physiological lung function test in use was dynamic spirometry with the Bernstein spirometer. Clinical exercise tests started a little later also in Tarina. In 1972, the Tarina Hospital became part of Kuopio Central Hospital.

In 1959, Erkki Vauramo started radiotherapy consultations at the Kuopio Department of Radiology. He worked as a physicist when, on the initiative two internal medicine physicians Martti Oka and Veli-Mikko Anttonen, he began to develop nuclear medicine activities. During 1961, physicist Ahti Rekonen joined the group. The isotope laboratory began operations on 9th February, 1962. Martti Oka and Reino Hiltunen were initially physicians in nuclear medicine. After them, Toivo Holopainen, a physician in the Department of Internal Medicine, became the long-term physician of the actual isotope laboratory. Initially, the focus of the nuclear medicine was on thyroid studies. Nodular goitre was common in Eastern Finland at that time. After the diagnostic studies, many patients received thyroid radioiodine treatment. At that time, the Schilling test, liver mapping with ^{195}Au colloid, and renography were also in use. Renographies were performed at their peak 1500 examinations a year, because Eastern Finns then had a lot of kidney stones, and renography was a good method to diagnose their effect on kidney function. The range of studies was expanded with limb blood flow studies and brain and kidney mappings. Of particular importance was the use of ^{85}Sr-chloride in the study of skeleton, especially the spine, and joints.

6.2 | Development of the specialty of Clinical Physiology and Nuclear Medicine at Kuopio University Hospital and Tarina Hospital

Kuopio Central Hospital was renamed and became Kuopio University Central Hospital in 1972, when the University of Kuopio was established. Until 1996, the activities of clinical physiology were located in both Puijo and Tarina Hospitals. In 1997, the last functions of clinical physiology were transferred together with the lung disease clinic from Tarina to Puijo Hospital. The date of establishment of the Clinical Physiology Laboratory in Kuopio can be defined as 16th October 1976, when the first specialist in this specialty was appointed to the laboratory. In this context, the functions of the nuclear medicine laboratory were also combined with clinical physiology. At that time, Esko Länsimies was the first specialist in clinical physiology appointed to the position of deputy chief physician. He was a long-term physician in charge of the Department of Clinical Physiology and Nuclear Medicine at Kuopio.

Already in the 1970s, a large and ambitious project, Data-ECG, was launched at Kuopio University. The construction of this regional ECG system began in Kuopio in 1972 and it was introduced in 1976. The data ECG system connected some health centers and other research institutes in the area to the ECG central unit of the University Computing Center via telephone lines. ECGs received in digital form were analysed, interpreted and retransmitted digitally via telephone lines to subscribers in response. Between 1976 and 1984, more than 170,000 ECG recordings were analysed in the Data ECG system. The Kuopio Data-ECG project collaborated with Dalhousie University in Halifax, Canada. The development of the analysis programmes had been done specifically in Halifax under the leadership of Pentti Rautaharju, a true pioneer in the field.

In the autumn of 1978, five laboratory rooms were repaired in the basement of Puijo Hospital for use in clinical physiology. The first facilities included the introduction of the first ECG long-term recording equipment and cardiac ultrasound imaging equipment. Sector imaging of the upper abdomen (liver, bile, pancreas, etc.) and thyroid was also initiated using the sector imaging device. Soon, the responsibility of these studies was transferred to the Department of Clinical Radiology, where equipment suitable for anatomical imaging was procured. At this stage, the number of clinical exercise tests also increased significantly and the range of studies diversified. Peripheral blood flow measurements and an orthostatic test were included in the study repertoire. Gastroenterological and urological studies were also developed in collaboration with clinicians.

In 1976 and 1979, the operations of the Tarina hospital expanded and further diversified. In 1979, 2300 dynamic spirometries were performed with a Bernstein spirometer in the Laboratory of Clinical Physiology at Tarina Hospital, and at the same time the bronchodilation response was determined by measuring before and after bronchodilator medication. Volumetric spirometries and diffusing capacity measurements were performed at a rate of about 1000 studies per year. Professors Erkki O. Terho and Hannu Tukiainen developed the studies of exposure experiments and methodology used in investigation of farmer's lung disease. The laboratory rooms had examination chambers in which various allergens could be administered. The bronchial responses of the subject to these were monitored by measuring respiratory outflow. In 1978, nearly 1200 exposure studies were performed.

6.3 | Activities of Clinical Physiology and Nuclear Medicine at Kuopio University Hospital

In 1990, the name of the hospital was changed again and since then it has been Kuopio University Hospital. In 1995, the total number of clinical physiological examinations was 27,769, of which 18,981 were resting ECGs. Of the other methods, the five most common were dynamic spirometry (3994 examinations), clinical exercise test (1417 examinations), diffusing capacity measurement (1214 examinations), lower limb arterial circulation measurement (610 examinations), and long-term ECG recording (456 examinations). The number of nuclear imaging and functional tests in 1995 was 2990 examinations, the most common of which were bone scans (1245 examinations), kidney examinations (505 examinations), cardiac examinations (466 examinations), brain scans (322 examinations) and lung ventilation and perfusion scans (293 examinations).

In addition to the continuous development of clinical physiological methods, noteworthy milestones have been the application of bone mineral density assessment methods in both clinical work and research. In the initial phase, physicist Paavo Karjalainen and professor Esko Alhava set up bone density measurements, which were used especially in women with possible bone loss. In the autumn of 1995, bone density measurement equipment based on the latest technology was introduced, which significantly improved the measurement accuracy and the availability of examinations. An exceptional number of 2177 bone mineral density measurements were made that year.

In the autumn of 1992, at the forefront, a three-detector gamma camera (Siemens MultiSPECT3) was purchased for the Department of Clinical Physiology at Kuopio University Hospital. Together with well-functioning radiochemistry, this opened up completely new dimensions for studying the body functions. With the new technology, there were also opportunities to include the studies brain functions and the mechanisms of various brain diseases.

The most recent major advances in nuclear medicine have been the introduction of our own PET/CT camera and the start of PET radiopharmaceutical production. PET scans, which started in 2005, were initially carried out with truck PET, but in 2012 a fixed PET/CT camera was installed on the premises of the clinical radiology facilities, which significantly improved the availability of the scans. In 2012, 497 PET scans were performed, and already 4 years later, in 2016, the limit of 1000 PET scans was exceeded. Facilities for the cyclotron and radiopharmaceutical laboratory required for radiopharmaceutical production were constructed in the new building. The first local ^{18}F-FDG production at the hospital took place on 1st June, 2016. The initiators of PET radiopharmaceutical production have been radiochemists Antti Mali and Pekka Poutiainen and pharmacist Jussi Tervonen. Mikko Hakulinen, a medical physicist who has been the project manager, has also played an important role in the planning phase of the operation. By spring 2020, in addition to ^{18}F-FDG, ^{18}F-fluorocholine, ^{18}F-flutemetamol, ^{18}F-florbetaben, ^{68}Ga-DOTANOC, ^{68}Ga-PSMA, ^{18}F-PSMA, ^{11}C-PiB, and ^{15}O-H_2O have been used for clinical PET imaging. Also ^{177}Lu-PSMA therapy for prostate cancer was started in 2020.

In 2017, the total number of clinical physiological examinations was 24,686, of which 15,439 were resting ECGs. Of the other methods, the five most common were long-term ECG recording (2780 examinations), dynamic spirometry (2664 examinations), diffusing capacity measurement (1637 examinations), clinical exercise test (1142 examinations), and lower limb arterial blood flow measurement (222 examinations). The number of isotope examinations and functional tests in 2017 was 3129. The most common of these were PET scans (1123 examinations), myocardial perfusion imaging (347 examinations), sentinel node imaging (238 examinations), brain receptor imaging (213 examinations), and bone scans (208 examinations). Bone mineral density measurements were made for 1961 patients.

6.4 | University status and medical training in Kuopio

The law on the Establishment of Kuopio University was enacted on March 25, 1966, and Kuopio University began its operations in 1972. In 1975, the hospital began to teach medicine. Along with the start of bachelor's studies, there were many methodological expansions. Therefore, it was not just a change of name to Kuopio University Central Hospital. Within the hospital, operations were oriented in a new way. For example, the previously unified central laboratory became divided into independent laboratories by specialty.

In the early days, the University of Kuopio invested in the position of part-time clinical physiology teacher. Quite soon, teaching in this specialty became accentuated, and associate professor Heikki Pekkarinen was appointed as full-time lecturer of clinical physiology. This was Finland's first full-time position for teaching clinical physiology. From the beginning, Esko Länsimies (Figure 14) was the head of the department. In 1998, he was nominated as the first Professor of Clinical Physiology at the University of Kuopio. Esko Vanninen (Figure 15) was appointed to professor's vacancy in 2004, and he had this position until 2010, when he took up full-time management positions at Kuopio University Hospital. In 2005, associate professor Hanna Mussalo took over the position of head of the Department of Clinical Physiology and Nuclear Medicine at Kuopio University Hospital, and to this day she has been responsible for the clinic's personnel and financial administration and the position of clinical chief physician. In 2010, Tomi Laitinen (Figure 16) was appointed as Professor of Clinical Physiology and Nuclear Medicine at the University of Eastern Finland. At the same time, he became the chief physician in charge of teaching and research in Clinical Physiology and Nuclear Medicine at Kuopio University Hospital.

The Department of Clinical Physiology and Nuclear Medicine in Kuopio has trained 21 specialists in the field, 31 medical physicists and two hospital chemists. Over the years, the Department of Clinical Physiology and Nuclear Medicine in Kuopio has organised many meetings and training events in its field, both independently and in cooperation with various associations.

6.5 | Research on Clinical Physiology and Nuclear Medicine in Kuopio

From the beginning, active scientific research has been an important factor in the development of clinical physiology and nuclear medicine in Kuopio. Especially in the early days, the methods that came into clinical use developed largely in parallel with the new methodology applied in research. In retrospect, it appears that the adoption of methods set up in research and development went smoothly. Thus, it is easy to see that research has had a very significant impact on the quality of patient work, providing advanced methods and practices for use in clinical work.

The field of clinical physiology and nuclear medicine has been one of the most successful medical specialties in research in Kuopio.

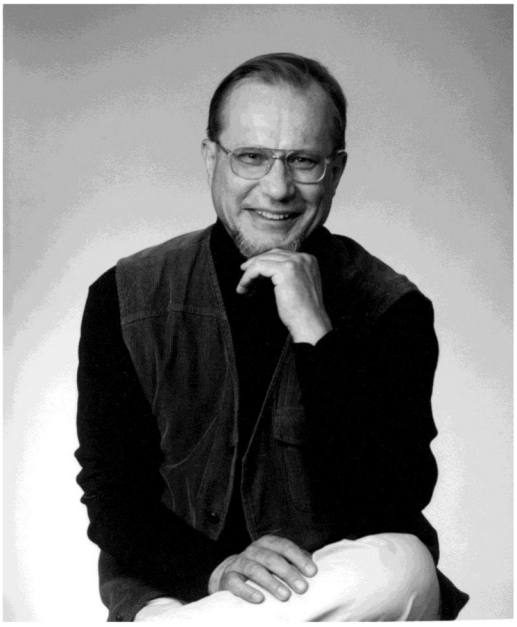


FIGURE 14 Professor Esko Länsimies



FIGURE 15 Professor Esko Vanninen

The method-oriented nature of the specialty, long-term and streamlined work in research, enthusiastic and competent staff, well-realised networking with partners in various fields, and close cooperation between the hospital and the university has made this possible. The advantage of the smaller university hospital and the



FIGURE 16 Professor Tomi Laitinen

adjacent university campus has been the opportunity to conduct research in a fruitful research environment, where experts from different fields can easily get to know each other, and the threshold for implementing cooperation is low. Clearly, over the years, research has been done on a wide variety of issues, but in the long run, three priority areas can be identified: (1) functional imaging, (2) musculoskeletal studies and (3) cardiovascular regulation studies. In research, networking has also been characteristic of the transition to the 21st century. The most important collaborative projects have been the Cardiovascular Risk in Young Finns Study and the Physical Activity and Nutrition in Children Study.

Of the staff in Clinical Physiology and Nuclear Medicine, eight physicians, 12 physicists, one radiochemist and one nurse have completed a doctorate. In addition to the dissertations of its own staff, the Department of Clinical Physiology and Nuclear Medicine has participated in numerous dissertation studies in other fields.

The work done in the hospital has changed in many ways and is still in transition. The generations of researchers have changed, there have been changes in research topics and the partners have changed. Yet the impact of the research tradition that has developed over the decades continues strongly in the current emphases of research.

6.6 | Clinical physiology in other hospitals surrounding Kuopio

In the **Central Finland Central Hospital** (Jyväskylä), internal medicine doctors had started to perform physiological examinations, such as clinical exercise tests and long-term ECG recordings. Pulmonologists

were responsible for lung function tests at Kinkomaa Hospital, and oncologists performed nuclear medicine examinations.

In the summer of 1990, the Department of Clinical Physiology was established, and in this connection two laboratory nurse positions were transferred from the clinical chemistry laboratory to the new unit. At the same time, the positions of nurse and primary nurse were transferred from the lung diseases outpatient clinic of Kinkomaa Hospital to the lung function laboratory and one senior house officer's position was changed to a resident's position. In addition, the positions of a hospital physicist, three radiological technicians and one laboratory nurse were transferred from the cancer and radiation outpatient clinic to the isotope laboratory.

Activities of the Department of Clinical Physiology began on 15 October 1990, when Tapani Parviainen started as the first chief physician of the unit. Petri Korkeila, Jari Töyry, Arja Uusitalo and Heikki Kuorikoski have acted as residents. Jarmo Toivanen was hospital physicist from 1990 to 1995 and Juha Vuorela since 1995. Associate professor Kirsi Timonen has been the chief physician since 2015. She also served as the unit's first department chief physician from 2011 to 2015.

The range of methodology has expanded with new methods within the framework of personnel and space resources. A significant improvement in the resources took place even before the turn of the millennium, when, in connection with the facilities of the Radiotherapy Hospital, a variety of activities could be transferred from the main hospital to the Radiotherapy Hospital's premises, where nuclear medicine was already operating. The final goal of a unified unit was achieved when, in connection with the closure of the operations of Kinkomaa Hospital in 2008, the lung function laboratory also moved to the facilities of the Radiotherapy Hospital.

In 2012, a PET-CT camera was acquired for the shared use with the radiotherapy clinic. PET examinations were started in the Central Finland Central Hospital as one of the first non-university central hospitals in Finland. For this purpose, the position of resident was changed to that of ward chief, with the special purpose of developing and promoting the performance of PET examinations in Central Finland. In 2012, a decision was made to build a completely new hospital in the Central Finland Hospital District. Initially, the hospital move was scheduled to take place in October or November 2020, but the coronavirus epidemic slowed hospital completion, and the time of migration to the hospital finally took place in January 2021. The Unit of Clinical Physiology and Nuclear Medicine is also located in the same unit as the Clinical Neurophysiology and Imaging Units. The biggest change was that clinical physiology and nuclear medicine no longer operated in several different locations, but all functions became together. Some equipment was renewed, and some moved from the old hospital. With the change, the Clinical Physiology and Nuclear Medicine unit received its own PET-CT camera.

The North Karelian Central Hospital (Joensuu) was established in 1953 as the first central hospital in Finland. In the 1950s, the World Health Organization sought to promote the introduction of nuclear medicine activities and awarded scholarships for this purpose. In 1958, this led the central hospital's chemist Olav Forssell to go to Harwell, UK, for a course in nuclear medicine. At that time, he also received practical training in London hospitals. Shortly thereafter, at the end of 1959, the laboratory started nuclear medicine activities with sample measurements. Paul Grönroos was the chief physician of the laboratory at that time. In the early days of the hospital, nuclear medicine belonged to laboratory activities and was partly done together with various specialties. Radioiodine therapies were started by the chief of internal medicine Helge Honkapohja.

Mapping was used in the nuclear medicine studies until Aristides Lambropoulos, chief physician of the laboratory, decided in 1976 to acquire the first gamma camera. Digital nuclear imaging began in 1980, when hospital physicist Aimo Hietanen connected a gamma camera to a computer. During Risto Härkönen's term as chief physician (1982–1989), the so-called the specialties of the undivided laboratory were separated into their own units. This gave birth to the Unit of Clinical Physiology, which also included nuclear medicine in accordance with the new specialty. At that stage, three-dimensional SPECT imaging of the heart was started, first with thallium in 1983. Later in 1987, myocardial perfusion imaging with technetium-MIBI was started in Joensuu as the first in Finland.

In 1990, Pentti Rautio started as chief physician. During his time, efforts were made to quantify and develop competence, which aimed at the high quality and availability in services. This led to the introduction of many new methods in this field. At that time, the incidence of the most common community diseases in North Karelia was clearly higher than in the rest of Finland, and more nuclear medicine studies were performed in proportion to the population in the area. Over the years, Risto Härkönen, Pentti Rautio, Pekka Turtiainen, Esa Kauppila and Hilda Westersund have been chief physicians of clinical physiology and nuclear medicine. Martti Larikka, Markku Walamies and Dmitri Jalovenko have been specialists. At the beginning of his career, Asko Seppänen also worked for a short time as chief physician.

Hybrid imaging began in North Karelia in 2016, when the benefits of hybrid imaging were already well established. Both SPECT-CT and PET-CT came into use in the same year. FDG-PET-CT has established its position in the diagnostics of many cancers, and PSMA-PET-CT for prostate cancer has already had time to significantly change treatment practices. In 2018, the number of PET-CT scans was just over 500, of which about 100 were PSMA scans. Bone imaging, iodine imaging, and somatostatin imaging of leucocytes in cancer patients are now performed as body SPET-CT hybrid imaging.

Clinical physiology, nuclear medicine and clinical neurophysiology have formed a joint unit since 1995. Since the beginning of 2016, all imaging specialties (clinical physiology and nuclear medicine, neurophysiology, radiology and pathology) have been the same service area. Since the start of the Siun Sote in 2017, the name has been the Imaging Center. Cooperation with the Savonlinna Nuclear Medicine Department has continued so that the North Karelia Central Hospital has been responsible for the medical part of nuclear medicine activities with reports and other services and the South Savo Central Hospital for radiation physics.

In the city center of Mikkeli, a hospital has been operating in the same place since 1845. In the **South Savo Central Hospital**, nuclear medicine facilities in the laboratory were taken into use in 1969. Simo Salminen had trained in nuclear medicine. He started his position in nuclear medicine on 4 March 1970.

In 1977, clinical physiology, nuclear medicine and clinical chemistry facilities were renovated and moved to the new premises of the hospital's third extension, which was completed in 1985. At the same time, a new gamma camera was acquired, which could already be used for tomography. After Simo Salminen retired in the early 1990s, the position of laboratory chief physician was not filled. The physicist made assessments of the isotope studies until in the late 1990s, when Hannele Jokivartio worked as a nuclear medicine physician in the isotope laboratory for about a year. The position of hospital physicist has been held by several physicists in the training phase. In 1996, associate professor Jari Heikkinen was appointed to the position of hospital physicist.

In the early 2000s, Tuula Tarkiainen started as the chief physician. The Department of Clinical Physiology and Nuclear Medicine was established on 1 January 2006. Before founding the Department of Clinical Physiology and Nuclear Medicine, Tuula Tarkiainen evaluated the situation of clinical physiology and isotope medicine in the hospital districts of South and East Savo. This provided a good basis for developing activities at Mikkeli Central Hospital. This development included concentration of clinical exercise tests and lung function tests to the Department of Clinical Physiology and Nuclear Medicine. Measurements of the autonomic nervous system were added to the methodology and by this constitutive work the range of studies was at a good national level.

Radiology, clinical physiology and nuclear medicine and pathology were administratively merged in 2007. At present, clinical physiology and neurophysiology form an administrative entity. Fusion of nuclear medicine studies with radiological imaging began in 2013, when the first SPECT-CT device was obtained.

Since 2014, Päivi Ylikangas, chief physician of the Eastern Finland Laboratory Center, has worked as a nuclear medicine physician in addition to her own work. The Department of Clinical Physiology and Nuclear Medicine has otherwise relied on the services of external consultants. Some of the exercise tests have been performed by the hospital's internal medicine physicians. Cardiologist Jori Nousiainen re-introduced myocardial perfusion studies in 2016.

7 | DEVELOPMENT OF CLINICAL PHYSIOLOGY IN OULU UNIVERSITY HOSPITAL AND SURROUNDING REGIONS

7.1 | Clinical physiology in the Oulu University Hospital

Unlike the other four university hospitals in our country, Oulu has not had clinical physiology and nuclear medicine as an independent specialty. Leo Hirvonen, the first professor of physiology at the University of Oulu, who moved from Turku, tried to strengthen the position of clinical physiology in Oulu. He and Tuomas Peltonen, professor of paediatrics at Turku, lectured on the key issues of clinical physiology at the University of Oulu in a physiology course.

The specialist training programme in clinical physiology and nuclear medicine under the new regulations was also established at the University of Oulu in the late 1990s. However, this ceased due to lack of resources. Before the abolition of subspecialties in the late 1990s, nuclear medicine was a limited specialty in clinical chemistry and radiology in addition to clinical physiology. In Oulu, the clinical chemistry laboratory was responsible for nuclear medicine at that time, and taught nuclear medicine with basic training in clinical chemistry. Later, activities of nuclear medicine were transferred to the Department of Radiology in Oulu, which established an additional training programme in nuclear medicine.

7.2 | Clinical physiology in central hospitals surrounding Oulu

Laboratory services and, as part of them, clinical physiology, has been organised at **Kainuu Central Hospital** in Kajaani since its establishment in 1969 in a so-called indivisible laboratory, and in part under the responsibility of clinical specialities. Nuclear medicine was started in 1978, when the first gamma camera outside Finland's university hospitals was acquired for the laboratory of Kainuu Central Hospital with the help of chief physician Aristides Lambropoulos. More resources were added to the development of clinical physiology and nuclear medicine starting from 1986, when hospital physicist Kimmo Leinonen became to the hospital district's laboratory, and a year after, when associate professor Esa Ahonen started as chief physician. From 2002, Pekka Ruuska continued as chief laboratory physician, followed by Heikki Aaltonen as director of the Kainuu NordLab Regional Laboratory.

The specialty of clinical physiology developed between 1987 and 2002 in the central hospital and the health centers of the hospital district as a functional entity by compiling common quality systems, costs, pricing and a quality manual as part of other laboratory activities.

In Kainuu, the planning of the Kainuu Administrative Experiment was launched in 2002–2004, which resulted in the implementation of the Kainuu Administrative Experiment and the Kainuu Provincial Administrative Experiment in 2005–2012. The change has enabled the integration of provincial services, which is also the aim of the national SOTE reform.

The specialty of clinical physiology and nuclear medicine was part of the Kainuu Hospital District's operations until it became part of the Kainuu County Consortium's operations from 2005, and in 2013 it became part of the Northern Finland Laboratory Center's NordLab. In 2016, the specialty became linked to the area of radiology as part of the Kainuu SOTE and later (from 2019) as part of diagnostic services, which includes services related to patient examinations.

In 2017, a new SPET/TT, bone density metre and other equipment were acquired. A new hospital will be under construction in Kainuu in 2019–2021, in connection with which the equipment base and methods will be renewed.

The activities of clinical physiology and nuclear medichave always taken place in the same premises at **Länsi-Pohja Central Hospital** in Kemi. In the early phase, hospital carried out some studies in nuclear medicine, and clinical stress tests were also performed there. However, there were no specialists in clinical physiology. Martti Larikka, who completed specialist training in clinical physiology at the University of Kuopio, started working in the summer of 1991 as a chief physician in the laboratory of Länsi-Pohja Central Hospital.

The operations of the specialty were part of the laboratory, and it became part of the Northern Finland Laboratory Center in 2013. However, the administration of clinical physiology and nuclear medicine returned to Länsi-Pohja Central Hospital in 2016, when it was merged into the Radiology Unit. The Länsi-Pohja Hospital District outsourced somatic medical services in 2018, and in this connection, the specialty became part of Mehiläinen Länsi-Pohja operations.

The nuclear imaging device was initially a gamma camera used for planar imaging, which was replaced by a SPECT camera suitable for tomography imaging in 1992 and SPECT-CT hybrid camera in 2005. SPECT-CT camera was upgraded in 2017. The methodology in clinical physiology includes clinical exercise tests, lung function tests and long-term recordings of ECG and blood pressure.

8 | MANAGEMENT OF CHANGE AND DEVELOPMENT

This article presents a wide range of past events that will have an impact on the future development of the specialty of clinical physiology and nuclear medicine in Finland. Previously chosen directions and policies will have a major impact on future thinking, practices, and service system structures, but in addition, general medical developments as well as technological and societal developments will bring change in the field of clinical physiology and nuclear medicine.

The Finnish pioneers in our specialty have been open-minded developers. A similar active pursuit of development will continue to be important in the field of clinical physiology and nuclear medicine. The generally strong technological developments inherent in modern times should not be ignored, especially in this kind of methodological field.

Managing change and development requires not only the active development of new methods but also the evaluation of their effectiveness. With new opportunities, new needs arise, a good example of which is the accurate diagnostics needed by individualised medicine and the assessment of individual treatment responses using objective methods. Artificial intelligence applications will play a key role here.

Applying special methods to expanding use increases costs in addition to benefits. The mere development and rapid introduction of new methods will not be enough in the future. In the future, the planning of activities will require an analytical examination of the research evidence also in terms of the cost/benefit ratio. On the other hand, the share of diagnostics in hospital costs is relatively small, and more accurate care-guiding diagnostics will become increasingly important as expensive treatments increase.

It is likely that big data-based research will increasingly be carried out and interpreted using artificial intelligence, while complex and expensive research will focus on expert units. This requires even more coordination in the standardisation of methods, information systems and training.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

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