

CANCER CARE AND RESEARCH AT KUOPIO UNIVERSITY HOSPITAL

ANNUAL REPORT 2019



CONTENTS

FOREWORD	2
KUOPIO UNIVERSITY HOSPITAL CANCER BOARD	2
KUOPIO UNIVERSITY HOSPITAL CANCER CARE ACCREDITATION PROCESS	.6
DIAGNOSTICS	3
Kuopio University Hospital's Clinical Pathology service receives FINAS accreditation	8
New MRI methods deliver improved accuracy in ovarian cancer diagnosis	(
New pre-operative MRI marking technique facilitates breast-conserving surgery	2
CANCER CARE	2
Minimally invasive surgery through robotic technology	2

A decade of image directed brachytherapy in the treatment of gynaecological cancers	16
More than 1,000 prostate cancer patients at KUH have benefited from stereotactic radiotherapy	17
CANCER RESEARCH	20
KUH now offering gene therapy for patients with ovarian cancer	20
New genomic approaches to studying leukaemia	22
A new treatment study of acute lymphoblastic leukaemia (ALL) in children and young adults is moving	
towards new treatments straight from the first-line therapies	24
The treatment of a rare childhood lymphoma, lymphoblastic lymphoma (LBL) is developing with	
international cooperation	26
IN NUMBERS – CANCER CARE AND RESEARCH AT KUH	28
PATIENT-CENTREDNESS	30
Patient Panels – an opportunity to shape services at KUH	30



Cancer is not just one disease but hundreds of different diseases. The more we look into the genetic processes underlying cancer, the more variation we find. While the aetiology of most cancers remains unknown, the genetic mechanisms, environmental and lifestyle factors and the risks associated with different infections are already well understood. Although much work remains to be done to identify the causes, significant progress continues to be made on treatments. In recent years, immunotherapies, PARP inhibitors and CAR-T therapies, have brought renewed hope for cancer patients. Advances in robotics are now allowing surgeons to operate with a greater degree of precision. Robotic radiotherapy treatment, too, allows clinicians to deliver more targeted therapy with fewer side effects. More precise imaging using MRI also allows for better planning of radiotherapy regimens, especially brachytherapy.

Planning for a National Cancer Centre first began in 2009 to ensure that Finland would remain a leading cancer treatment provider in this fast-moving and challenging field. That mission was finally accomplished in October 2019, when all Finnish hospital districts became signatories to the National Cancer Centre agreement. However, much remains to be done at the national level before the centre is operationally read. Regional services were first launched in 2018.

Screening, diagnostics, management and follow up are co-ordinated by regional centres, set up on direction of the Ministry of Social Affairs and Health, in Finland's

special catchment areas. In the Kuopio University
Hospital special catchment area, these services are
under the control of FICAN East. All regional healthcare districts, i.e. PSSHP, KSSHP, Siun sote, Essote and
Sosteri, along with the University of Eastern Finland,
operate in accordance with the agreement.

Each year, some 5,100 new cancer diagnoses are made in our region. The local population experiences the highest levels of morbidity in Finland, presenting a particular challenge for the clinicians. Although the rate of incidence is not predicted to rise, the Finnish Cancer Registry forecast shows that the number of new diagnoses is expected to increase by 34%. This means that by 2035 there will be 46,100 new cancer cases in Finland, compared with 34,000 today. The rise in the number of cases can be largely attributed to an ageing population. The number of cancer survivors is also expected to rise. Our healthcare system faces significant challenges, not only due to the rising number of cancer cases but also because care is becoming more personalised. Fresh new solutions are needed to make this affordable. Research will have a key role to play in facilitating service provision. In our vision, research will be integrated into every step of each individual patient's cancer pathway. Indeed, research is one of the most important tasks entrusted to the regional and national Cancer Centres.

The success of our research activities depends on highquality regional and national cooperation. If we are to deliver the best outcomes for cancer patients and ensure equality in service provision, management must be based on high-quality diagnostic services, standardised treatment regimens and national clinical guidelines, as well as consider the patients' own wishes and preferences. To ensure quality, each treatment plan should be discussed at a multidisciplinary team meeting.

In order to evaluate and improve the quality of cancer services we offer at Kuopio University Hospital, we have applied for membership of the Organisation of European Cancer Institutes (OECI) and are currently going through the accreditation process. The University Hospitals in Helsinki, Turku and Tampere have already received accreditation. This annual report represents one milestone on our way towards achieving accreditation. It covers our cancer services in the course of 2019 and lists some of the highlights in the fields of diagnostics, management and research.

To continue this work, we should do it together with good collaboration and supporting each other for the best outcomes of our patients,

Dr Maarit Anttila MD, Ph.D., Clinical Lead and Acting Director, FICAN East; Head of Department, KUH Gynaecology

KUOPIO UNIVERSITY HOSPITAL CANCER BOARD





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Heikki Miettinen Hospital Director, Hospital Administration



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Clinical Lead and Acting Director,
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Anna-Liisa Levonen Vice-Dean Faculty of Health Sciences



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Department of Medicine

THE CANCER CARE **ACCREDITATION PROCESS**



FICAN East in brief

FICAN East is one of the five regional cancer centres, each operating within their own special catchment areas (SCA). FICAN East operates within the Kuopio University Hospital SCA. FICAN East's core areas of activity are the harmonisation of clinical protocols, ensuring equality of service provision within the region and facilitating research, development and innovation in collaboration with other regional cancer centres and FICAN the national coordinating centre

www.ficaneast.fi



Kuopio University Hospital Cancer Centre in brief

KUH Cancer Centre is a network organisation that brings together cancer care, research and education and training activities. Formed by Kuopio University Hospital and the University of Eastern Finland, it is a key part of FICAN East.



OECI accreditation in brief

The purpose of the Organisation of European Cancer Institutes' accreditation programme is to support European cancer centres as they develop their services and quality assurance processes by implementing OECI's qualitative standards across cancer care delivery, research and audit.

www.oeci.eu/Accreditation/





2016

• April 2016, a national cancer centre remit working group is established

2017

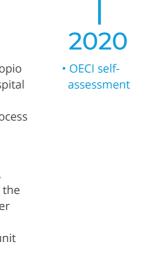
- The National Cancer Centre Remit Working Group meets
- FICAN East launched

2018

- June 2018, **Kuopio University** Hospital receives OECI membership
- June 2018, agreement on the establishment and structure of FICAN East concluded

- June 2019, Kuopio University Hospital commences application process for OECI accreditation
- October 2019, agreement on the National Cancer Centre and coordinating unit concluded
- November 2019, **KUH Cancer Centre** Board commences work







DIAGNOSTICS

Kuopio University Hospital's Clinical Pathology service receives FINAS accreditation.

The Finnish Accreditation Service has granted accreditation to the KUH Diagnostic Imaging Centre's Clinical Pathology service. The accreditatio recognises the excellent service provided by the centre and the quality of the work being done here.





Text Johanna Eronen, KUH Communications Photos Riikka Myöhänen, KUH Communications

The Clinical Pathology service is responsible for preparing and analysing all tissue and cell samples obtained from patients at the hospital. The accreditation encompasses all histology, cytology and postmortem reporting carried out by the laboratory team.

"What the accreditation achieves is that it ensures our procedures are standardised, our methods meet the required standards and the quality of our output is evaluated not only internally but also by external quality assurance bodies," explains Sanna Kirjavainen, Medical Cell Biologist.

"It means that doctors, patients and our external clients alike can be confident that what they are accessing is a high-quality service that's committed to ongoing development."

The department also needs the accreditation if it is to take part in national and international research collaborations. There are currently 22 pathology laboratories in Finland, seven of which are FINAS accredited.

Sanna Kirjavainen, Medical Cell Biologist and Ollipekka Terävä, Laboratory Nurse.

The accreditation process is carried out on the basis of internationally established criteria. During the process, the accrediting body evaluates the laboratory's management system as well as clinical performance. Most importantly, the standard is designed to reflect the needs of patients and customers. Feedback and complaints are recorded, reviewed and ultimately used to improve the service.

In total, the accreditation process lasted just over 12 months and included a visit by two external assessors. The assessment was carried out in accordance with SFS-EN ISO15189:2013, which complies with the SFS-EN ISO 17011:201 on conformity assessments.

DIAGNOSTIC

New MRI methods deliver improved accuracy in ovarian cancer diagnosis.

Ovarian cancer is known to be associated with poor clinical outcomes. New targeted therapies have been sought to achieve improved treatment efficacy and to extend survival. Rapid advances in treatment will need to be matched by new imaging techniques.

Text UEF PhD media release / Outi Nikunen Photo Riikka Myöhänen, KUH Communications

Epithelial ovarian cancer accounts for more deaths than any other cancer of the female reproductive system. Due to the absence of early signs and symptoms, epithelial ovarian cancer is usually diagnosed at an advanced stage. Signs and symptoms include unusual abdominal discomfort and pain, changes in urinary and bowel habits, weight loss and a palpable abdominal mass. A screening programme would facilitate early detection but unfortunately, no reliable test currently exists. Dr Auni Lindgren's PhD thesis showed that functional MRI (fMRI), diffusion weighted imaging (DWI) and dynamic contrast enhanced MRI (DCE-MRI) offer more accurate diagnosis of ovarian cancers.

"First of all, it's important to note that ovarian cancer is not just one disease. There is huge molecular, histological and biological variation within it. Given this diversity, when it comes to treatment, we are likely to be moving towards greater individualisation in the future," Dr Lindgren says.

The purpose of Dr Lindgren's thesis was to investigate whether multivariate MRI methods could be applied to ovarian cancer. CT scanning remains the first-line imaging technique for the diagnosis and staging of ovarian cancer internationally.

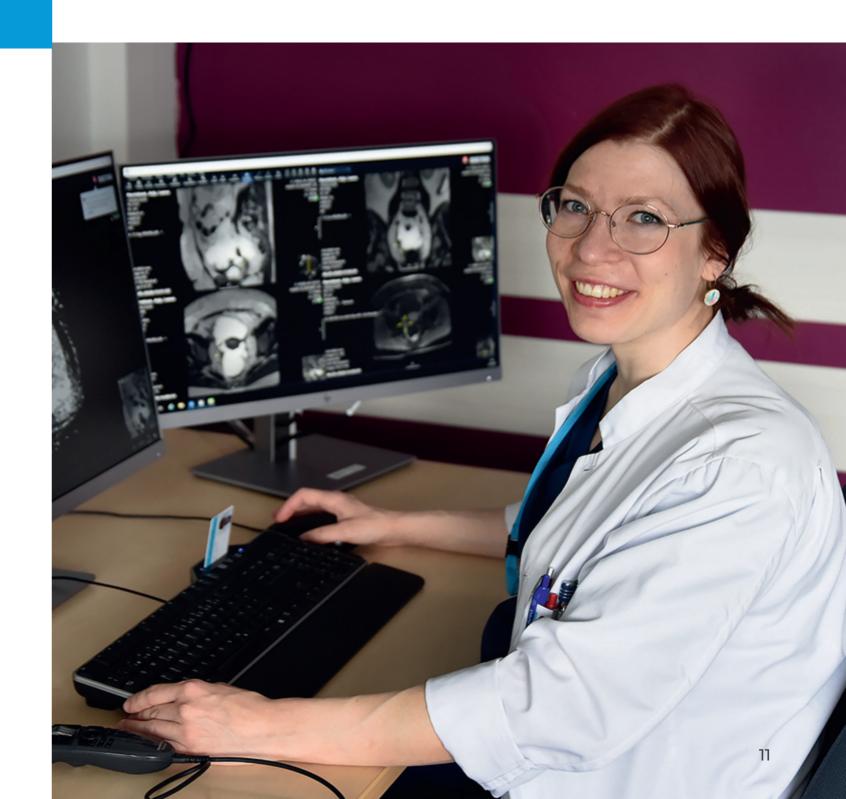
Ongoing technological advances have meant that the availability and accessibility of MRI has improved significantly. The thesis compared CT and MRI scans to investigate whether the latter offers potential to yield more detailed pre-operative information regarding tumour characteristics to support therapeutic decision making.

According to the research findings, lower ADC values correlate with more aggressive tumour behaviours and are associated with a poorer prognosis. A further finding was that in a dynamic contrast-enhanced (DCE) imaging study, high-grade serous ovarian cancers were associated with higher volume transfer constant values (Ktrans) of contrast agent from plasma to extracellular extravascular space but were also predictors of better cytoreductive surgery outcomes. DCE imaging parameters Ktrans and Kep (a rate constant of transferred contrast agent from EES to plasma) were lower in patients with elevated expression levels of hypoxia-inducible factor 1 alpha (HIF-1α).

Lindgren's thesis demonstrates that new functional magnetic imaging methods may serve as surrogate markers allowing a more detailed characterisation of ovarian cancer.

"We believe that more accurate imaging techniques will play an increasingly important role in patient care. Cancer treatments are constantly improving and the general trend is towards increasingly personalised care. As the results showed significant promise, we are using the imaging techniques investigated as part of my PhD research in Dr Hanna Sallinen's Phase 1 ovarian cancer gene therapy trial currently underway at Kuopio University Hospital. We also plan to take a close look at the benefits offered by functional imaging in the diagnosis of gynaecological cancers," explained Dr Auni Lindgren, Consultant in Obstetrics and Gynaecology.

Dr Lindgren successfully defended her PhD thesis on *Multiparametric magnetic resonance imaging in epithelial ovarian cancer* was at the Faculty of Medical Sciences in October 2019.



DIAGNOSTICS

New pre-operative MRI marking technique enabling breast-conserving surgery.

Breast cancer is the most common cancer in women and the leading cause of death for working-age women. Surgery is the first line of treatment for breast cancer. Radiotherapy and drug treatments as necessary. The majority of patients can be treated with breast-conserving surgery followed by adjuvant radiotherapy. Plastic surgery techniques now allow conservative excision techniques to be used even for highgrade, multifocal and multicentric cancers. A new MRI marking technique developed at Kuopio University Hospital allows breast radiology specialists to mark multifocal and multicentric tumours in preparation for surgery.

Text Sarianna Joukainen / Outi Nikunen Photos Riikka Myöhänen, KUH Communications

The aim of breast cancer surgery is to remove all malignant tissue using wide excision margins in a single operation while retaining the natural appearance and symmetry of the breasts. Oncoplastic surgical techniques are used when the surgical site is large in relation to overall breast size. This surgical subspecialty uses plastic surgery techniques, including re-shaping and flaps to replace the volume lost during excision.

Breast surgery is planned in advance guided by histology and imaging results. Any non-palpable changes must be identified using imaging and marked prior to surgery. Mammography and ultrasound are the primary imaging tools used in breast cancer management.

Patient positioning, SupineMRI.



Dr Sarianna Joukainen, Consultant Plastic Surgeon and Breast Cancer Surgery Lead at Kuopio University Hospital.

Where necessary, these are complemented with MRI, the most sensitive imaging modality for identifying breast cancer. Breast cancer is often multifocal and multicentric and a significant proportion of additional lesions go undetected by mammography and ultrasonography. Until now, accurately locating and marking additional MRI-identified malignant changes has been challenging due to the fact that patient positioning is different for imaging and surgical purposes. In contrast with surgery, which is performed in the supine position with the breasts against the thoracic wall, diagnostic MRI imaging is performed in the prone position with the breasts pendant.

At KUH, thoracic radiologists and plastic surgeons joined forces to find solutions to this commonly occurring problem. The multidisciplinary team developed a method where the tissue changes identified during a prone MRI are localised and marked using a supine MRI scan that mimics the patient positioning for surgery. In 2017–2018, they carried out a prospective study to assess the suitability of this method for use in clinical settings. The results were published in the European Journal of Radiology in June 2019.

"What the study showed was the SupineMRI method works well and provides a more accurate picture of where the tumours are located and their side than a prone diagnostic MRI, which exaggerates their size. The SupineMRI method is a new tool for clinical teams to localise and mark tissues changes that can only be identified through MRI," explains Dr Sarianna Joukainen, Consultant Plastic Surgeon and Breast Cancer Surgery Lead at Kuopio University Hospital.

A follow-up study is currently underway. It's designed to compare the outcomes of SupineMRI oncoplastic surgeries with traditional wire-guided US or mammogram marking or oncoplastic operations where no lesion marking was required.



CANCER CARE

Minimally invasive surgery through robotic technology.

Robotic minimally invasive surgery was launched at KUH in February 2016, with the introduction of the state-of-the-art DaVinci Xi system.

Text Maarit Anttila Photos Riikka Myöhänen, KUH Communications

Although KUH was the last Finnish university hospital to introduce robotic surgery, it has worked hard to catch up since then. In the past four years, more than 1,000 operations have been carried out using DaVinci Xi. The robot-assisted system was first used for a gynaecological procedure and by October 2019, the 500th gynaecological operation was completed.

In robot-assisted minimally invasive surgery, 3D imaging allows for an improved view of the operating field, while the machine helps to steady the surgeon's hand. Robot-assisted surgical systems are particularly well

Robot-assisted surgeries, total

400
350
350
300
262
101
100
121

Gynaecology
Cynaecology
150
100
50
50
2016
2017
2018
2019

KUH Urology team, from left to right, Sirkku Siltari, Arto Salonen, Erja Ponkkonen, Petri Sammasmaa, Anniina Henttinen.

from left to right, Sirkku Siltari, Arto Salonen, Erja Ponkkonen, Petri Sammasmaa,

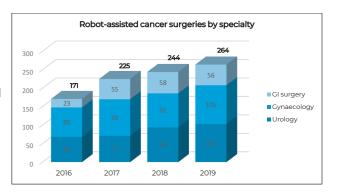


KUH Gynaecology team, left to right, Maarit Anttila, Hanna Sallinen, Maija-Liisa Fröberg, Minna Sopo, Saila Rautiainen and Henna Kärkkäinen.

suited for cancer surgery in the pelvic cavity because of the limited space available.

The technique uses small incisions to facilitate surgery, which aids recovery and allows patients to be discharged earlier. Other benefits include reduced blood loss, reduced analgesia and reduced risk of open surgery.

At KUH, robot-assisted minimally invasive techniques have primarily been used for uterine, cervical, rectal and prostate cancer surgery. Increasingly, however, it is also being used for bladder and renal cancers.



KUH GI Surgery team, left to right, Samipetteri Laine, Katja Vänskä, Anne Fagerström, Niina Holopainen, Petra Nissinen, Maijeli Rönkkö, Liina Kärkkäinen and Riitta Mikkonen.



CANCER CARE

A decade of image-guided brachytherapy in the treatment of gynaecological cancers.

Brachytherapy is a form of radiotherapy that complements external beam radiation and allows clinicians to deliver doses of radiation directly to the primary tumour bed. Previously, it has been difficult for clinicians to deliver sufficient doses of radiation to large tumours using external beam radiotherapy while minimising adverse effects on surrounding organs.

Text Maarit Anttila Photo Riikka Myöhänen, KUH Communications

MRI-guided radiotherapy treatment planning in combination with advanced applicators has delivered significant improvements in the treatment of locally advanced or recurrent gynaecological cancers. MRI-guided brachytherapy for gynaecological cancers was launched on 9 February 2009. The 10th anniversary of the treatment was celebrated in 2019. During that decade, 130 cervical cancer and 50 other gynaecological patients received brachytherapy in Kuopio. In 2019, 45 women with cervical cancers received brachytherapy, while 34 women received prophylactic MRI-guided cervical radiation therapy.

In 2019, an average of six brachytherapy needles

were used per treatment fraction in 2019, while in 2009, when the technique was newly adopted and the team were still learning it, two needles per treatment fraction were used. The advances made in this area are clearly evident from the reduction in total radiation doses given to patients and improvements in local control. A multidisciplinary team is essential for the brachytherapy delivery. With several years of experience, the team now offers a tertiary and national service.

From left to right, Maarit Anttila, Henna Rissanen, Marjaana Boman, Anu Palomaa, Tuomas Viren, Ester Jääskeläinen and Jan-Erik Palmgren.

CANCER CARE

More than 1,000 prostate cancer patients at KUH have benefited from stereotactic radiotherapy.

Kuopio University Hospital first launched a stereotactic body radiation therapy service in 2012 when it became first hospital in the Nordic region to acquire the CyberKnife system. Now, more than a thousand patients have benefitted from the treatment, which has shown itself to be both highly effective and safe.

Text Johanna Eronen, KYS viestintä Photos Riikka Myöhänen, Sakari Partanen, KYS viestintä

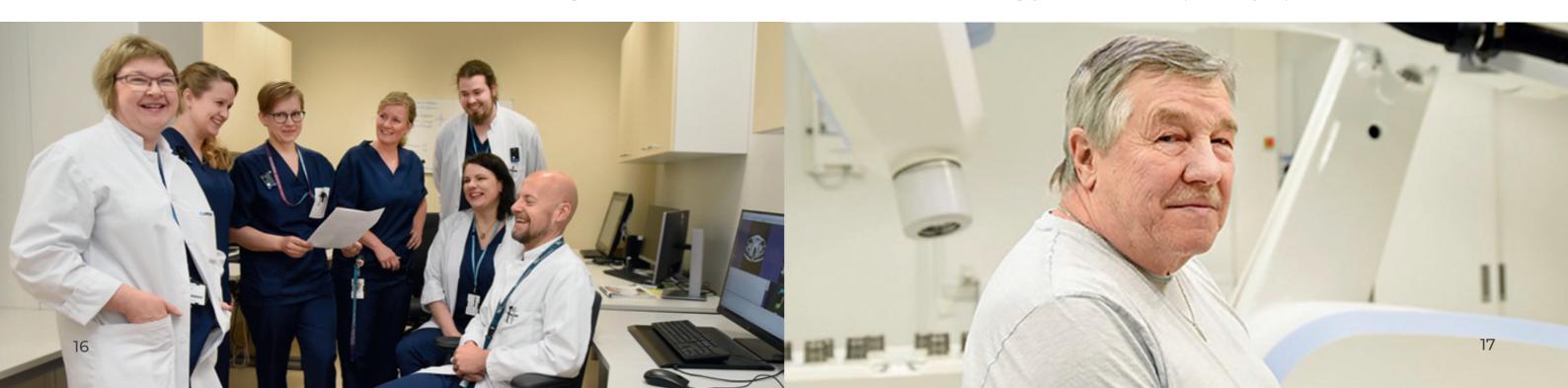
Teemu Rautiainen from Muuruvesi, close to Kuopio, received prostate cancer treatment at Kuopio University Hospital in March. He was offered brachytherapy as tests showed his cancer had not spread and the specialist coordinating his care did not recommend surgery. The treatment will be administered over five sessions. Once this initial course has been completed, the situation will be reviewed.

"It's all gone really well. They talked me through everything," Teemu Rautiainen says, clearly pleased with the progress he is making. He says he is happy with how the treatment is going.

Each session lasts about 30 minutes. During that time, he is asked to lie down and remain still, while the CyberKnife does its work.

"They've put a nice landscape photo on the ceiling above me, and I've tended to look at that while I wait. I wouldn't mind a different picture every once in a while, though," he says with a chuckle.

Teemu Rautiainen is receiving CyberKnife treatment at Kuopio University Hospital.



Along with Teemu Rautiainen, around 1,000 other men have received prostate cancer treatment at Kuopio University Hospital. They come from all over Finland, with around a quarter of the referrals received from outside the hospital's special catchment area, including from abroad.

The team at KUH are continuing to actively evaluate the efficacy of the treatment they offer. The results of a long-term surveillance study offer new data on the treatment of patients diagnosed with a more aggressive type of prostate cancer. Kristiina Vuolukka.

"Stereotactic body radiation therapy has been shown to be an excellent treatment option for patients with localised low or intermediate prostate cancer. We've just completed a five-year analysis of treatment efficacy, and it looks like it also works well for high risk patients with localised disease," explains Dr Kristiina Vuolukka a specialist at KUH Oncology Centre.

Dr Kristiina Vuolukka and KUH researchers found that SBRT is an effective treatment for patients with high-risk localised prostate cancer.





Radiographers Kari Tervo (left) and Aija Juutilainen make sure Teemu Rautiainen is well looked after during his visit.

Well tolerated and effective

CyberKnife's high level of precision limits the volume of radiation delivered to the healthy tissue surrounding the targeted area and adverse effects are usually low.

Some patients experience more frequent urination or urinary hesitancy, even after the first treatment. Changes to bowel habits are generally limited. All in all, any acute adverse effects patients experience during or after treatment are usually mild and self-limiting.

"The benefit of CyberKnife in comparison with other precision radiation therapy delivery techniques is that CyberKnife will remain focused on the targeted area even if the patient or the treatment site moves. Accuracy is improved too as the therapy can be delivered with sub-millimetre accuracy from a number of different directions. Typical treatment areas include the brain, spine, prostate and lungs," says Jan Seppälä, Senior Medical Phycisist.

During hypofractionated stereotatic radiotherapy, large doses of radiation are delivered over a limited number of sessions. In comparison with traditional forms of prostate cancer radiotherapy, it is a more gentle, straightforward and cost-effective alternative.

Typically, 36–39 treatment sessions are required as

part of traditional radiotherapy. With hypofractionated radiotherapy, the same effect can be achieved in just five sessions.

Due to its greater degree of accuracy, it allows larger single doses to delivered in fewer sessions. These higher doses are more effective at destroying cancer cells than smaller doses delivered over a greater number of sessions, making the treatment more effective.

Prostate cancer is the most common cancer in men in Finland, with around 5,000 new cases diagnosed each year. The average age at diagnosis is 70.



Hormone therapy, radiotherapy and surgery are used to treat prostate cancer. The doctor discusses the treatment plan with the patient. The plan is based on the size of the tumour, growth pattern and staging as well as the patient's age and any underlying medical conditions they may have. In some cases, the decision may be to just monitor the situation, particularly if treatment would not improve the prognosis.

KUH now offering gene therapy for patients with ovarian cancer.

A novel gene therapy developed at Kuopio University Hospital is now being offered to patients with ovarian, fallopian tube cancer and primary peritoneal cancer.



Text Ulla Kaltiala Photo Raija Törrönen, University of Eastern Finland

This clinical trial marks the first time that this drug is tested in humans. Patients receive the new gene therapy alongside standard therapies.

"Ultimately, what we're trying to do is achieve improved outcomes for patients with recurrent cancer," explains Dr Hanna Sallinen, an Obstetrician and Gynaecologist with a specialist interest in gynaecological cancers.

The investigational drug is administered intravenously one week before the chemotherapy. The patients taking part in the trial are given adenovirus-mediated gene therapy, which uses a viral vector to insert the therapeutic gene to the target. All of the virus's pathogenic

Dr Hanna Sallinen, Consultant Gynaecologist and Obstetrician.

properties have been eliminated to allow them to be used as a vector. The therapeutic gene is a soluble VEGF receptor that will prevent angiogenesis and lymphangiogenesis.

"This means that we can slow down cancer progression because the tumour cannot grow without a blood supply. The reason we're also trying to stop the growth of lymphatic vessels is that these allow the cancer to spread," Sallinen explains.

It's not often that doctors get to administer a treatment they themselves have developed. Dr Hanna Sallinen first began work on a new gene therapy in 2003 when she was a member of Academy Professor Seppo Ylä-Herttuala's group at the A.I. Virtanen Institute. She gained her PhD in 2010. The safety and efficacy of this treatment have been scrutinised for well over a decade. Commencing a clinical trial for a new gene therapy has also involved a long regulatory process. The gene therapy is manufactured by Finvector Vision Therapies, a research-led private enterprise.

"So far, the results from pre-clinical studies show that it is delivering a reduction in tumour size. The treatment has also been found to be safe and well-tolerated. Any side effects are milder than those commonly associated with traditional forms of chemotherapy. We keep our patients at the hospital for a few days after we've administered the treatment but, other than tat, it does not limit your life in any way.

Ovarian cancer is associated with a poorer prognosis than other gynaecological cancers as due to the nonspecific signs and symptoms involved, diagnosis is often delayed.

"What we tend to see is that when women do present to a doctor, the cancer has often already spread quite extensively. A proportion of patients fail to respond well to chemotherapy, which means that there is a significant need for more targeted treatments," Sallinen points out.

"Ovarian cancer is rarely associated with just one tumour. They're often found in a number of locations in the peritoneum, but with this delivery mechanism the gene therapy is capable of targeting them all. In KUH's catchment area, around 80 new cases are diagnosed annually.

"In addition to these 80 patients, we also offer treatment to patients with recurrent cancer. For many of our patients this is not the first or even the second time they're receiving treatment.

The new gene therapy is being tested in women with recurrent ovarian cancer. It is also suitable for women with recurrent fallopian tube cancer or primary peritoneal cancer as these cancers share many similarities and are treated using the same therapies. Only patients capable of tolerating traditional chemotherapy were recruited for the trial. One group of subjects will receive a placebo treatment and act as a control for the trial.

"So far, patients have been incredibly positive about the trial. They've been really interested in the possibilities that gene therapy offers and we've had people getting in touch from quite far away wanting to take part," Dr Sallinen explains.

At this phase of the trial, patients are given a single gene transfer.

"As this is a Phase 1 trial, the focus is on demonstrating that the treatment is safe, but we're also hopeful we will see evidence of tumour reduction too. In subsequent trials, the plan is to administer repeated doses of the gene therapy and to use two soluble VEGF receptors as a combination therapy to more effectively inhibit angiogenesis and lymphangiogenesis.

Original news item:

Patients in Kuopio receive novel gene therapy for ovarian cancer, February 2019.



Find out more:

New gene therapy for ovarian cancer launched in Kuopio, June 2019

"This is a gene therapy first" – Dr Hanna Sallinen is living every clinical researcher's dream, Mediuutiset news, November 2019.

New genomic approaches to studying leukaemia.

Associate Professor Merja Heinäniemi's research group at the University of Finland's Department of Biomedicine are applying the latest genomic approaches to investigate links between the biology of childhood leukaemia and prognosis.

Text Ulla Kaltiala Photo Raija Törrönen, University of Eastern Finland

Current research projects focus on genomic measurements taken at an early stage in the treatment process to identify new prognostic features. The researchers use different cell and animal models to understand their underlying mechanisms. The COSMOS project funded by the Academy of Finland investigates new subtypes of leukaemia, while a separate project run by the department, which benefits from a major grant from the Finnish Cancer Foundation along with the GEPARD project that forms part of the European EraPerMed network turns its attention to subtypes defined by specific gene fusions. The GEPARD project is coordinated by Olli Lohi from the University of Tampere, while the other two projects are overseen by Merja Heinäniemi.

"We can use the new genomic analysis techniques available to us to map the mutations present in the genome as a whole and to generate complete transcriptional profiles of the cells. Moreover, we are able to use single cell sequencing to shed light on what actually

happens during treatment using samples we collect to monitor the patients' response to it.

Heinäniemi's group has collected samples for genomic analysis, investigated leukaemia cell function, prognostic features and treatment efficacy in collaboration with paediatric oncology teams at Kuopio University Hospital and Tampere University Hospital. Alongside Olli Lohi's team, the team have also collaborated closely with genomic and preclinical murine modelling experts in Sweden and Germany.

The funding from the Jane and Aatos Erkko Foundation will also allow the team to carry out wider genomic mapping of all new cases of childhood leukaemia diagnosed at KUH and TAYS.

Petri Pölönen, Doctoral Researcher, with Associate Professor Merja Heinäniemi.



A new treatment study of acute lymphoblastic leukaemia (ALL) in children and young adults is moving towards new treatments straight from the first-line therapies.

More than 90 per cent of children and young people with acute lymphoblastic leukaemia (ALL) can be cured.

Text Kaisa Vepsäläinen Photo Riikka Myöhänen, KYS Viestintä

The development of treatment has been a true success story, the current challenges of which relate to improving the treatment of adult patients, developing the treatment of patients with slow response and certain cytogenetically abnormal leukaemias, as well as reducing adverse effects in patients with a most favourable prognosis. To promote these goals, new precision treatments and advanced cell therapies have to be introduced alongside chemotherapy. To achieve this, a novel international treatment protocol for ALL, ALLTogether is being implemented.

As of autumn 2020, children and young adults (1-45 yrs of age) with acute lymphatic leukaemia will be treated in accordance with the novel ALLTogether treatment programme, i.e. protocol, in which Finland is participating with 13 other European countries. Professor Mervi Taskinen is the principal investigator of the treatment programme in Finland. In Kuopio University Hospital (KUH), Kaisa Vepsäläinen, M.D., Ph.D., associate chief physician and Marja Pyörälä, M.D., Ph.D, associate chief physician, are in charge of the treatment protocol.

NOPHO cooperation between Nordic paediatric oncologists played a strong role in generating ALLTogether. The framework of ALLTogether protocol was built on the basis of previous data and treatment outcomes in the countries participating in the research. The patients participating in the protocol shall be referred to treatment in accordance with genetic leukaemia cell mutations and initial treatment response.

Approximately one thousand patients are treated in compliance with the ALLTogether protocol every year. The protocol will be implemented from five to seven years, after which the outcomes will be published with access for all. The opportunity to enter a total of approximately 6,500 patients into the ALLTogether protocol provides significant data about the care and treatment of patients with ALL. Extending treatment consortiums accelerates the development of treatment

The goal of the treatment protocol is to improve the outcome of children and young adults with ALL by



ALLTogether treatment study is the largest treatment and study protocol combining children and young adults.

testing a number of randomised and non-randomised interventions. Since failure of the current treatment of ALL in children and young adults are due to both under- and overtreatment, both under- and over-treatment adverse outcomes are targeted. The study protocol provides more personalised treatment and new innovative interventions for the so-called undertreated patients, i.e. a group of patients for whom traditional chemotherapy is insufficient, and who have a high risk of therapy-failure by death from disease. At the moment those patients are treated by increasing

the amount of conventional chemotherapy. Within this treatment protocol they are offered innovative treatments, such as an antibody-targeted treatment, CAR-T-cell therapy, and Tyrosine-kinase inhibitor, imatinib for the patients with targetable genetic lesions. On the other hand, it is quite possible that currently some of the patients are overtreated and they could be cured with less treatment. Therefore, the goal of the treatment protocol is to reduce serious adverse effects to patients with a favourable prognosis, and to enhance the quality of life.

KUH children and adult haematology team (left): Kaisa Vepsäläinen, M.D., Ph.D, associate chief physician, Marja Pyörälä M.D., Ph.D, associate chief physician and M.D., Ph.D, chief physician Taru Kuittinen.



The treatment of a rare childhood lymphoma, lymphoblastic lymphoma (LBL) is developing with international cooperation.

Lymphoblastic lymphoma is a rapidly progressing, aggressive lymphoma, with permanent cure rate of children and young adults up to 90% at the moment. The problem, however, with this type of lymphoma is that in the event of recurrence, it is almost impossible to cure with traditional treatments - only less than 15% of children can be cured under the circumstances. The primary goal of the novel treatment protocol is to reduce the risk of relapse.



In Finland, the principal investigator of the LBL2018 Research and Treatment Protocol is Kaisa Vepsäläinen, M.D., Ph.D, associate chief physician, Kuopio University Hospital, Unit of paediatric haematology.

Text Kaisa Vepsäläinen Photo Riikka Myöhänen, KYS Viestintä

LBL2018 Research and Treatment Protocol is a scientific research programme of the treatment for lymphoblastic lymphoma in children and adolescents, a cooperative effort of 20 European and non-European countries. The programme was approved in Europe in autumn 2018 and in Finland it has started in 2020. In Kuopio University Hospital (KUH), similarly to the other paediatric haematology-oncology units in Finland, nearly all children and adolescents are treated in compliance with international research and treatment

protocols. LBL2018 being one example of such international multi-centre projects.

In Finland, the principal investigator of the LBL2018 Research and Treatment Protocol is Kaisa Vepsäläinen, M.D., Ph.D, associate chief physician, Kuopio University Hospital, Unit of paediatric haematology.

The new LBL2018 Treatment Protocol enables more specific diagnostis and risk classification, thus iden-



LBL2018 Research and Treatment Protocol is a scientific research programme of treatment for lymphoblastic lymphoma in children and adolescents, a cooperative effort of 20 European and non-European countries.

tifying more precisely the patients who are at a particularly high risk of recurrence of the disease. The most significant change, in comparison to the earlier treatment, is the more precise risk group classification, which determines the choice of treatment intensity. Risk group stratification (standard risk / high risk) is based on the immunophenotype of the tumour and genetic (including NOTCH1 + FBXW7 mutations) findings in addition to the stage of disease.

Furthermore, the aim of the randomized questions are to evaluate, whether increased intensity of treatment can reduce central nervous system relapses in all the patients and improve disease-free survival of patients with high overall relapse risk.

Improved paediatric cancer treatment outcomes have led to a paradoxical situation: the smaller the group of patients with relapses, the more difficult it is to de-

monstrate the effect of therapeutic intervention in the shrinking group of patients. Lymphoblastic lymphoma represents a rare lymphoma sub-group: in Finland, the estimated number of patients is between five and ten patients a year. Within the LBL2018 research and treatment protocol, approximately 650 children and adolescents will be diagnosed and treated during the next five years. The international cooperation and analysis of shared data help to identify risk factors and develop treatments for rare cancers faster than before.

IN NUMBERS – CANCER CARE AND RESEARCH AT KUH



International peer-reviewed publications

Publications
with
IF > 10

Clinical trials 49

Patientsparticipating

Cancer research budget

3.2 million euro

Clinical trial subject visits 487

in clinical trials

102



Diagnose patients 2 764

Total cost of cancer medication

Radiation fractions delivered

9 million euro

17 437

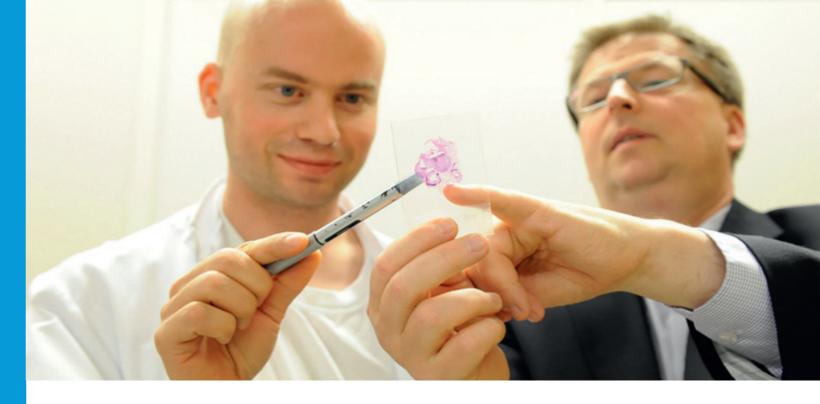
New radiotherapy patients

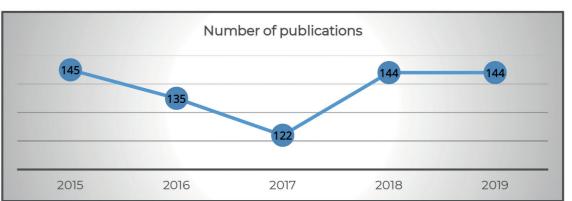
1 733

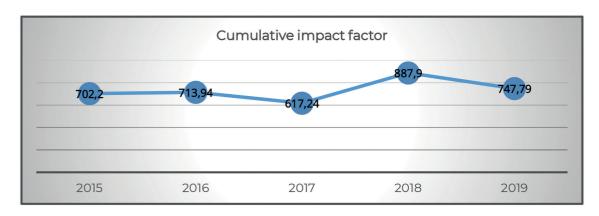
Number of drug administrations 19 275

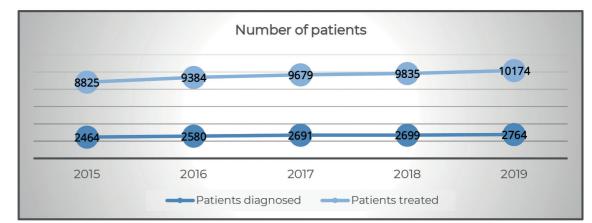
Clinic appointments

20 611









PATIENT - CENTREDNESS

Patient Panels – an opportunity to shape services at KUH.

This year saw the introduction of new Patient Panels at KUH, as the previously established hospital-wide panel was complemented with the addition of departmental panels, including one set up at the Oncology Centre. The panels are an opportunity for service users and their families to contribute their views on service design, evaluation and monitoring.



Text Johanna Eronen, KUH Communications
Photo Sakari Partanen, KUH Communications

First established in April 2019, the Oncology Centre Patient Panel met five times. Leena Martikainen has sat on the panel from its inception. At the meetings, the panel have covered a number of issues, including interaction between patients and staff.

"We discussed how meaningful that first encounter is when you've just been diagnosed with a serious illness. How that one moment will change your life forever and how we'd like the healthcare professionals to approach it," Martikainen says.

Senior Nurse Niina Kela-Korhonen says the Patient Panel has allowed the staff to develop a better understanding of the role psychosocial support plays in the delivery of holistic cancer care. Panel members have particularly highlighted the need for that support when the diagnosis is first received by the patient.

"We need increased clarity of the types of support available, more holistic care coordination, staff training and greater collaboration between primary and secondary care," Niina Kela-Korhonen points out.

"We will use the contributions made by our panel members to draw up a psychosocial support development plan that's tailored to the needs of cancer patients."

Collaboration between patients and professionals delivers optimal care

For Leena Martikainen, the Patient Panel has been a valuable opportunity to get involved and shape the service she uses. She would like to encourage other patients and their families and friends to take part too.

"This has been an opportunity for us as patients to share our views on how the service is run, what works and what doesn't.

What matters is that we can use our own personal experiences to improve the standards of care provided here."

She makes it clear that patients and their families using the service have their own unique perspective on the service that's different from how the staff working there see it. We know that to achieve the best outcomes, it's vital that we take account of the views of both patients and staff.

As a healthcare professional, Niina Kela-Korhonen feels that the Patient Panel has allowed her to view her own work in a completely new way.

"The Patient Panel is a genuine opportunity to see our service through our patients' eyes and gives me lots of new ideas for how we can develop it further.

For Leena Martikainen, the meetings and getting to know new people has been a valuable source of peer support.

"Although we all have our own unique story, we still have something in common with one another. We have received first rate care at KUH, and we're all responding to treatment in our own way. I firmly believe that, if we work together, we can make change happen. We can make sure that no one is left isolated following a cancer diagnosis, that everyone has a treatment pathway in place and the right contact details they can use to access support.

The first KUH Patient Panel
was set up in 2016. In 2019,
service-specific panels were
set up at the Oncology Centre,
Heart Centre, Acute Services
and the Child and Adolescent
Centre of Excellence. At the end of November,
a call will go out for members to take part in
the Psychiatry Patient Panel.

Taina Haikarainen (left) and Leena Martikainen met at the KUH Oncology Centre Patient Panel.

KYS Syövänhoitokeskus KUH Cancer Centre



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