The Norwegian Cancer Society – National Expert Group for Radiotherapy Research

Background

The overall aim of cancer care is to cure the disease while minimizing the treatment related complications, i.e. live longer and better. Radiotherapy is a main pillar in modern multimodal cancer treatment. Fifty percent of all cancer patients will require radiotherapy during the course of their disease and around 14 000 Norwegian cancer patients undergo radiotherapy annually [1]. During the last 30 years the proportion of long-term cancer survivors in Norway has increased from 50 to 75%, likely due to improved diagnostics, and more effective treatments. Today, more than 300 000 individuals are alive 5 or more years after their cancer diagnosis and are defined as long-term survivors. However, many long-term survivors have late effects of treatment which impact their quality of life [2].

Since the implementation of "Nasjonal kreftplan" in 1997 [3], major resources have been allocated in order to decentralize radiotherapy in Norway, ensuring equal access to radiotherapy for all patients [4]. These resources have not been accompanied by investments in necessary radiotherapy research [5]. In 2021 the Norwegian health authorities published an action plan for integration of clinical research into standard patient care in order to increase the proportion of patients included in clinical trials [6]. The planned National Expert Group for Radiotherapy Research fits well into this initiative.

Introduction

Advances in clinical radiotherapy are made through clinical trials and translational research, as well as technological development.

Interdisciplinary collaboration between hospitals and academic institutions is important in order to offer equal treatment and participation in evidence-generating clinical trials to all cancer patients. Patient participation in clinical trials is known to improve cancer care and prognosis [7]. Collaboration with established international networks and institutions is essential to expand knowledge and to achieve better patient outcomes. Inspirationally for this project, a similar national platform (Danish Comprehensive Cancer Center (DCCC) radiotherapy) was established in Denmark in 2018 [8].

Photon therapy is today delivered at nine radiotherapy departments distributed across the four health regions in Norway. Decentralization of radiotherapy is important to avoid geographical variations in utilization rates [4], ensuring equal access to optimal cancer treatment. During the next years, new radiotherapy facilities will open, including proton therapy centers at the university hospitals in Oslo and Bergen. Proton therapy is a new treatment option in Norway, and the two proton facilities will offer treatment to patients from all health regions. The total capacity for proton therapy in Norway will be three gantries, treating almost 900 patients per year or 6 % of the radiotherapy patients. Proton therapy is regarded standard treatment for selected patient groups, including children with cancer. However, for most radiotherapy indications, clinical evidence for the utility of proton therapy is still missing. Indications for proton therapy are likely to increase with the introduction of next-generation proton therapy facilities. The establishment of proton therapy in Norway implies increased focus on radiotherapy research in general, aiming to improve cancer control with reduced normal tissue complications [9]. The majority of patients (75 %) treated with proton therapy will be included in clinical studies or protocols. To reach this number, a robust national infrastructure is essential to ensure adequate and widespread inclusion. The clinical studies will mainly be carried out as multi-center studies, which will require national and international collaboration [10].

A Norwegian proton- and radiotherapy registry, including data from all Norwegian departments engaged in radiotherapy, is under construction. The registry will be of great importance for the initiation and conduction of clinical studies, providing detailed radiotherapy data from all radiotherapy departments in Norway and long-term follow-up data for proton patients. Preparation of clinical studies will be interdisciplinary with involvement of relevant expertise from clinical research, translational research and universities. In the National Expert Group for Radiotherapy Research, all professionals will be present to build an interactive research platform including translational research.

The publicly financed comprehensive healthcare system in Norway provides a unique possibility, as well as an obligation, to produce high quality comparative clinical data on radiotherapy that could impact health care decisions.

Aim

The overall aim of the National Expert Group for Radiotherapy Research is by strengthening radiotherapy research and increase the inclusion in clinical trials, to improve prognosis for cancer patients with better survival and better quality of life.

Objectives

1. To establish a comprehensive, multidisciplinary National Expert Group dedicated to radiotherapy research.
2. To advance clinical and translational research in radiotherapy in Norway.
3. To strengthen infrastructure that supports clinical and translational research collaborations within radiotherapy.
4. To initiate clinical trials and translational research projects focusing on proton and photon therapy.
5. To increase the participation of Norwegian patients from all four health regions in clinical radiotherapy trials.
6. To improve treatment outcomes, specifically in terms of tumor control and patient survival, while reducing toxicity and enhancing the quality of life for cancer patients.

Methodological approach and project plan

In order to reach our goals, we will establish a multidisciplinary National Expert Group for Radiotherapy Research. The expert group will include members from radiotherapy departments and academic institutions in all four Norwegian health regions.

In this application, we have defined five distinct work packages (WP); two WPs focusing on the national infrastructure, two WPs for clinical trials and one WP for translational research. The planned deliveries and milestones for each WP are described below. Collaboration between the WPs is important, as well as collaboration with international organizations and institutions.

National and international collaborating organizations:

Norwegian infrastructure Clinical Research in Norway (NorCRIN), Network in Radiation Oncology (NIRO), Norwegian Center for Clinical Cancer Research (MATRIX), Norwegian Radiation and Nuclear Safety Authority (DSA)-KVIST, European Society for Therapeutic Radiotherapy and Oncology (ESTRO), European Particle Therapy Network (EPTN), European Organization for Research and Treatment of Cancer (EORTC), DigiCore/One, Danish Center for Particle Therapy (DCPT), The Skandion Clinic, University Medical Center Groningen (UMCG) and national and international multidisciplinary cancer groups

WP1: Establish a National Expert Group for Radiotherapy Research

Work package leader: Åse Bratland
Work package members: Mirjam Delange Alsaker, Marianne Brydøy, Grete May Engeseth, Marianne Grønlie Guren, Taran Paulsen Hellebust, Thomas Kilvær, Ingvil Mjaaland, Kjersti Øvrum Skipar, Camilla Hanquist Stokkevåg (all).

Description of work:

A comprehensive framework for clinical trial counseling and administration, organized as a national multidisciplinary expert group, serves as a platform for networking and to enhance high-quality

radiotherapy research. The infrastructure of the expert group includes management and administration of the group and is essential to reach the goals.

All Norwegian radiotherapy departments, including the two proton facilities, as well as relevant academic institutions contributing to radiotherapy competence and scientific activity, will be invited to take part in the National expert group. This widespread involvement will enhance national collaboration and overall radiotherapy expertise and promote equitable access to clinical trials in radiotherapy for all cancer patients in Norway.
Dissemination of activities and results from the radiotherapy research community is important to stimulate scientists to take part in the national research field.

Deliverables:
D1: Initiate a multidisciplinary national collaboration in radiotherapy research comprising key personnel from proton and radiotherapy facilities and academic institutions
D2: Establish a website for radiotherapy research
D3: Increase collaboration in translational radiotherapy research
D4: Initiate more clinical radiotherapy trials and increase the number of patients participating in the trials. Approximately 75% of patients treated with protons will be included in clinical protocols/trials

Milestones:
Y1: Establish a National Expert Group for Radiotherapy Research
Y2-4: Arrange annual conferences and workshops, support initiation of clinical radiotherapy trials, and dissemination and publishing of research results

WP2: Radiotherapy research infrastructure

Work package leader: Kjersti Øvrum Skipar
Work package members: All

Description of work:
Adequate infrastructure for radiotherapy research is imperative to generate high quality clinical trials and real-world data, and to facilitate widespread dissemination and implementation of study results into clinical practice [5]. Additionally, this will stimulate pre-clinical research that will address and test new treatment strategies translatable into future clinical trials. This WP aims to ensure the establishment of crucial national infrastructure for radiotherapy clinical and translational research.
The introduction of proton therapy in Norway anticipates the inclusion of most patients in clinical trials. It has initiated the creation of a Norwegian proton and radiotherapy registry encompassing both proton and photon therapy. This registry will serve as a distinctive framework for radiotherapy research, incorporating clinical and radiotherapy data, as well as important outcomes such as patient-centered metrics. Registry implementation will extend to all Norwegian radiotherapy departments, and data will be obtained based on a written informed consent. This consent may allow linkage to medical images and biological material facilitating translational research. In addition, pre-clinical proton therapy infrastructures are being established in Oslo and Bergen. Implementation of informed consent procedures, as well as routines for long-term follow-up registration, are crucial infrastructural measures facilitating radiotherapy research in general.
In collaboration with national tumor groups and national and international stakeholders, the network will support the design of evidence-generating clinical trials addressing significant topics in radiotherapy

To streamline and facilitate clinical trial development and conduction, the network will establish standardized templates for protocol procedures (NorCRIN). This may include electronic clinical report forms (eCRF), electronic patient reported outcome measures (ePROM), statistical analysis plan and procedures for quality assurance (QA), data management, and monitoring. Furthermore, to facilitate translational research, overall standard operating procedures for administration of biological material

and medical images will be developed. There will be access to templates and procedures through the web site. Information will be shared at meetings and workshops.

Deliverables:
D1: Implement the Norwegian proton and radiotherapy registry at radiotherapy centers
D2: Use the National Expert Group for Radiotherapy Research for competence sharing
D3: Establish standardized templates for clinical trial setup suitable for radiotherapy research
D4: Facilitate translational research by ensuring widespread implementation of informed consent procedures, and develop procedures for medical images and biological material
D5: Develop a collaboration platform with pre-clinical environments and infrastructures in Oslo and Bergen

Milestones:
Y1: Cross-disciplinary competence sharing through the National Expert Group for Radiotherapy Research
Y2: Norwegian proton- and radiotherapy registry is established, and data is collected
Y2-3: Standardized templates for clinical trial setup and conduction are developed, and administrative procedures facilitating translational research are established
Y4: Number of Norwegian patients included in radiotherapy trials is increased

WP3: Clinical trials in relevant tumor groups

Work package leader: Marianne Brydøy
Work package members: All

Description of work:
Several clinical radiotherapy studies are ongoing or soon to be started in Norway. In general, the trials exampled below aim to improve outcome, reduce side effects, and to provide more individualized radiotherapy based on individual risk factors and biomarkers. Some of the studies form a solid basis for further studies as we move forward into a new era with proton therapy being available in Norway. In the following, we give brief descriptions of ongoing studies and relevant protocols and clinical trials in planning. Complete descriptions and protocols will be developed for applications for funding from different sources both nationally (KLINBEFORSK, Cancer Society grants, Regional Health trust etc) and internationally (EU-grants).

Reduction of treatment burden by more individualized patient selection for radiotherapy and limitation of the target volume is explored in the *Natural trial (NCT03646955)* and *T-REX trial (NCT05634889)* in breast cancer. Dose de-escalation will be investigated in early-stage cervical cancer in the *Embrace low risk* study.

Adaptive treatment, i.e adaptation during the treatment course based on anatomical changes, often enables individualized margins and reduced target volumes. The *Plan of the Day study (NCT05634681)* for cervical cancer utilizes a library of individual plans, and in the *TNT-Record study (NCT05883800)* in rectal cancer, artificial intelligence is applied for daily online adaption.
Dose escalation may improve efficacy in radioresistant tumours. In the planned *Radpaint-3 trial* in head and neck cancer patients, higher dose is given to radioresistant tumor areas identified by FDG-PET. Patients treated with both photons and protons will be included in this trial.

Combining radiotherapy with systemic therapies may enhance efficacy. The *Ravina* trial *(NCT05724602)* studies the efficacy of an anti-apoptosis agonist in elderly head and neck patients. Other combinations studies are the *Taormina trial (NCT05377047)* investigating combining stereotactic ablative RT with systemic treatment in oligometastatic breast cancer, and the *Triplex (NCT05223647)* and *ABC-X (NCT03340129) trials* where radiotherapy is added to immuno(chemo)therapy for small cell lung cancer and melanoma brain metastasis, respectively.

Several ongoing studies explore giving immunotherapy during or following radiotherapy for cancers in the lung, head and neck, skin and anus.
Addressing tumor hypoxia is an important objective in radiotherapy research to overcome resistance. The *Metoxy-lacc trial (NCT04275713)* explores alteration in hypoxia-related gene expression when adding metformin to chemoradiotherapy in cervical cancer, while hypoxic profiling in treatment selection is focus in the *Dahanca 30 trial (NCT02661152)* for head and neck cancer patients.
There is a need for clinical proton therapy studies to define indications and to select the right patients for proton therapy. So far, most studies have been on tumors of the brain and head and neck. *PRO-GLIO* is a phase III trial initiated in Norway *(NCT05190172)* recruiting patients with brain tumors (IDH-positive diffuse glioma grade II and III) in Norway and Sweden. The patients are randomized between photon treatment at their regional hospital and proton treatment at the Skandion clinic in Sweden. Safety, health related quality of life (HRQOL) and neuropsychological issues are explored.

A national randomized study for reirradiation comparing protons and photons is planned for recurrent or second primary head and neck cancer (*Riphron study*), with dysphagia as primary end point. For mucosal melanoma of the head and neck a phase 1 study, assessing the safety and toxicity of hypofractionated, dose-escalated postoperative proton therapy is in preparation. Other national protocols addressing treatment selection for meningiomas, and head and neck (oral cavity) cancer patients as well as other relevant sites are under discussion. Advancements in robust planning and adaption techniques (WP5) allow for clinical studies to explore indication for proton therapy in areas where organ motion may be challenging (i.e lung and pelvis).Prospective collection of PROM and patient reported experience measures (PREM) in studies will be encouraged (WP2, 5).

The Norwegian Multidisciplinary Cancer Groups will contribute to inclusion of patients in ongoing, international clinical trials and they have expressed interest in the following protocols: *DAHANCA 35* (pharynx and larynx) and *PROTIS* (sinonasal) for head and neck cancer, *PROTECT* for oesophageal cancer, possibly *SWANCA* and *PRORECT* for anal and rectal cancer, *PRO-Hodgkin* for Hodgkin lymphoma, and *PRO-THYM* for thymoma.

Deliverables:
D1: Provide a comprehensive overview over clinical radiotherapy trials in Norway
D2: Increase inclusion of Norwegian cancer patients from all four health regions in ongoing, multicentre radiotherapy trials
D3: Include patients in international multicentre proton studies
D3: Increase the number of radiotherapy trials with PROMs and PREMs
D5: Finalize protocols for proton therapy studies
D6: Initiate new clinical radiotherapy trials in relevant cancers

Milestones:
Y1: Publish and regularly update a comprehensive overview over clinical radiotherapy trials available for Norwegian cancer patients on the web site
Y1-2-3: Initiate and conduct clinical planned radiotherapy trials. Prepare new protocols
Y2-3: Include patients in international proton therapy protocols and trials
Y4: Conduct clinical trials and disseminate results

WP4: Clinical trials for general indications or patient groups

Work package leader: Thomas Kilvær
Work package members: All

Description of work:
Most patients receiving radiotherapy are not eligible for conventional tumor specific clinical trials, and many important general issues in radiotherapy remain unanswered. WP4 will facilitate initiation of

tumor agnostic studies and studies across tumor types, enabling us to standardize patient care, answer unmet needs in radiotherapy, and ultimately benefit patients who will receive improved treatment. The newly initiated *PALLSOFT* study is an example of a nationwide study that aims to answer an important question in radiotherapy, namely the optimal dose for palliative treatment of pelvic soft tissue tumors.

The availability and use of innovative radiotherapy techniques, e.g. stereotactic brain (SRS) and body (SBRT) radiotherapy varies between centers. Moreover, the advent of proton therapy in Norway underscores the need for tailored strategies to determine the most effective treatment for individual patients. Thus, to ensure equal treatment for Norwegian cancer patients there is a need for national consensus on implementation and use when new techniques are established. The established network (WP1) will be in a unique position to harmonize and develop procedures enabling national centers to initiate current and new innovative treatment techniques.

Current radiotherapy planning does not adequately consider late side effects. Hence, acquiring detailed information on the combined radiation exposure from radiotherapy and imaging is a prerequisite when considering new prospective treatment planning paradigms – particularly for children. Further, current knowledge of treatment outcomes combined with the potential of selected toxicity of proton therapy can include patient perspectives in treatment planning.

To reach the goal of 75% of patients receiving proton therapy being enrolled in clinical trials, new innovative trial designs are needed. A basket trial design may act as framework for studies irrespective of tumor type. The framework would comprise several smaller trials recruiting patients and evaluating results separately or pooled according to the endpoint of interest. Tumor agnostic endpoints will typically be related to tolerability and late effects but could also include tumor control and survival and/or other measures of response related to biomarkers. Thematic areas for tumor agnostic trials include, but are not limited to, SBRT dose optimization, reirradiation and oligoprogression/oligometastatic disease.

Deliverables:
D1: Establish and arrange meetings on general topics relevant to further the work defined in the WP
D2: Develop a national consensus guideline for SRS/SBRT in Norway through mapping its use in all Norwegian radiotherapy facilities
D3: Update current clinical radiotherapy protocols to include risk of late side effects
D4: Develop a national consensus guideline and design prospective registration protocols for proton therapy in children and young adults
D5: Develop a basket trial design for specific tumor agnostic indications
D6: Establish a national consensus and prospective registration of radiotherapy for oligometastatic and oligoprogressive disease
D7: Decision-support tool/framework for patient involvement in assessment of late effects

Milestones:
Y1: National consensus guideline and prospective registration protocol for proton therapy in children developed
Y1: Methodological approach for optimizing paediatric radiotherapy
Y1-2: Collect and summarize SRS/SBRT protocols including dose restraints to organs at risk
Y3: Consensus guideline for SRS/SBRT in Norway developed
Y2-4: Consensus guideline and prospective registration protocol for proton therapy in young adults developed

WP5: Medical physics translational research in clinical radiotherapy

Work package leaders: Grete May Engeseth, Taran Paulsen Hellebust, Camilla Hanquist Stokkevåg
Work package members: All

Description of work:
Integration of translational research into radiotherapy is essential to our understanding of radiobiological mechanisms. Through developing and implementing innovative treatment strategies and technologies, we can ultimately achieve enhanced effectiveness and safety in cancer treatment. In radiotherapy, there are unmet needs to identify reliable biomarkers of treatment response and short- and long-term toxicity. Further, highly precise molecular and image-based markers are a prerequisite for biological treatment adaptation and evaluation of biological effects. Ongoing research focuses on imaging biomarkers, adaptive radiotherapy, model-based prediction and treatment selection strategies, and development of novel biological optimization strategies for photon and proton therapy. The implementation of automation and artificial intelligence (AI) in radiotherapy is currently in its early stages [11] requiring research efforts to advance and refine.

High quality medical imaging (e.g. CT, PET, and MR) prior to and during treatment is a prerequisite for modern highly conformal radiotherapy. Highly conformal dose distribution is often achieved with the inherent risk of missing the target volume because of motion uncertainties like breathing, bowel movements, bladder filling and volume changes during treatment. Robust planning is even more important with protons due to the physical properties and risk of change in dose distributions as the protons trespass various tissues in the body. However, optimal utilization of imaging modalities still presents challenges, and protocols defining the application of motion management and adaptive radiotherapy remain to be developed and validated.

The use of functional imaging biomarkers in individualized radiotherapy planning and treatment adaptation is only beginning to surface. Functional imaging comprises the use of imaging methods to visualize biological or physiological characteristics of tumors and normal tissue and mainly refers to metabolic imaging by positron emission tomography (PET) and functional MRI sequences [12, 13, 14, 15]. E.g. functional imaging biomarkers linked to radioresistance, will enable us to selectively increase dose to the most radioresistant tumor sub-volumes while maintaining acceptable doses to surrounding normal tissues [16]. On the other hand, biomarkers linked to increased radiosensitivity can support radiotherapy dose-reduction and thereby decrease toxicity [17]. Furthermore, there are considerable knowledge gaps related to the use of imaging biomarkers in early detection of radiation-induced toxicity, and research is still required to develop and implement new approaches clinically (e.g. EMINENCE project *(NCT04612075)*.

Improved methods for investigating tissue and liquid biomarkers to predict patient response and guide personalized radiotherapy, are needed [18, 19]. By identifying specific biomolecular signatures, the aim is to develop robust predictive models that can be used to optimize radiotherapy outcomes and minimize adverse reactions. Moreover, novel hypotheses will be tested in pre-clinical model systems, including patient-derived materials, using the coming pre-clinical facilities in Oslo and Bergen. This includes novel combination therapies with new molecular targeted drugs. Finally, these activities will be integrated with the exploration of imaging biomarkers and biophysical modelling (mentioned below).

Predictive modelling plays a pivotal role in radiotherapy and requires input from detailed follow-up on tumor control (TCP) and toxicity (normal tissue complication probability, NTCP) for a specific patient population [20, 21]. Such models can be used to optimize the treatment plan, for patient selection (ex. protons vs photons), and to inform the individual patient about estimated risks as part of shared decision-making. National studies on model development and validation for head and neck cancer are ongoing. The models will be employed in treatment selection across patients with head and neck cancer and developed for further indications (WP3,4).

Proton radiation exhibits an elevated relative biological effectiveness (RBE) compared to conventional photon-based therapy. The latter feature is quantifiable through the linear energy transfer (LET), and through radiobiological models accounting for the RBE. To investigate whether inclusion of LET/RBE could refine prediction, analysis of retrospective and prospectively collected outcome data (e.g. *Pro-Glio*) and future clinical proton studies are required [22]. Therefore, collection of LET/RBE data will

be conducted in all clinical proton studies initiated by our group (WP3,4). Furthermore, biological optimization research protocols to reduce risk of toxicity and/or increase tumor control will be explored (e.g. from ongoing BioProton study).

The automation and use of AI in treatment planning streamlines the complex process of optimizing radiation treatment plans. Dicom and follow-up data from patients will be used as input to novel software generating high-quality state-of-art photon and proton treatment plans based on national treatment planning protocols. Moreover, the automated strategies will be applied in comparative planning across techniques, also including NTCP models validated on Norwegian patients.

Deliverables:
D1: Form an advisory board aiming to provide input on translational research opportunities to clinicians during the development of clinical radiotherapy studies
D2: To establish a framework for translational and pre-clinical research including patient materials and cell and animal model systems
D3: Establish national framework defining applications for motion management and adaptive radiotherapy for relevant disease sites and range of radiotherapy modalities
D4: Establish a framework for automation in radiotherapy, including automatic comparative treatment planning and model-based patient selection
D5: Increase the number of studies including translational research, i.e. predictive modelling and response evaluation, adaptive approaches, motion management and biological optimization
D6: Develop research protocols for biological optimization and evaluation in proton therapy

Milestones:
Y1: Advisory board for translational research is established
Y1-4: National protocols for model-based selection to proton therapy (for various sites)
Y1-4: National protocols for adaptive photon and proton therapy (for various sites)
Y2: Shared software for automated treatment planning
Y2: Protocols for biological optimization developed and tested in-silico
Y2-4: Harmonized CT, MR and PET acquisition framework for national clinical trials and methods for image analyses to be used in biomarker development

Project infrastructure and organization
This application has been developed as a collaboration between ten persons involved in radiotherapy research, further referred to as the application group. The four health regions in Norway (Helse Nord HF, Helse Midt HF, Helse Vest HF and Helse Sør-Øst HF) are represented in this group, with participants from six radiotherapy departments (University hospital of Northern Norway, St Olavs hospital Trondheim University Hospital, Haukeland University Hospital, Stavanger University Hospital, Telemark Hospital Trust and Oslo University Hospital) and universities in Bergen and Oslo. The members represent different disciplines in radiotherapy research and clinical practice, and they are involved in international collaboration.

Radiotherapy research and clinical radiotherapy trials are important to improve cancer care. A National expert group for radiotherapy research will develop a platform where translational and clinical research are integrated. Multidisciplinary collaboration and transparency are necessary to initiate and conduct more clinical radiotherapy trials in Norway.

Based on the deliveries and milestones described in the WPs, a National Expert Group for Radiotherapy Research will be established. An open invitation will be sent to hospitals and academic institutions involved in radiotherapy research. The expert group brings different professions together in a national framework contributing to knowledge sharing and competence building. A well constructed national infrastructure will support the collaboration. The national approach is central to ensure equal inclusion of patients from all over Norway. The WPs describe the planned activities and timelines for the expert group. A united Norwegian academic community can facilitate access to international research collaboration and participation in international multicenter studies.

Organization

All ten representatives of the application group will be part of a steering committee, led by the main applicant (ÅB, OUS). The user representative, Morten Bryn, will also be a part of the steering committee.

The National Expert Group for Radiotherapy Research (NERR) will have a management team consisting of a coordinator, the main applicant and 2-3 members appointed by the application group, rotating annually.

NERR will collaborate with the proton centres and facilitate development, initiation and inclusion in the national proton therapy trials.

Figure 1.

This figure shows the distribution of existing radiotherapy departments (red) and radiotherapy departments under construction (gray) including proton therapy facilities (yellow) in Norway

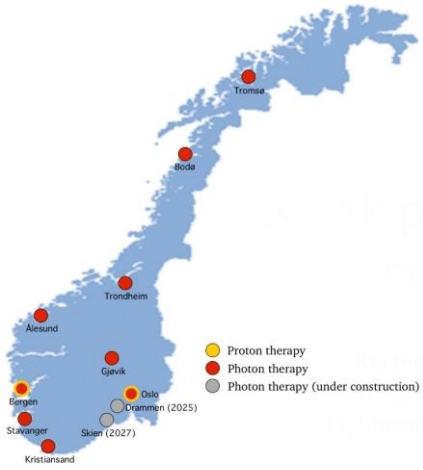
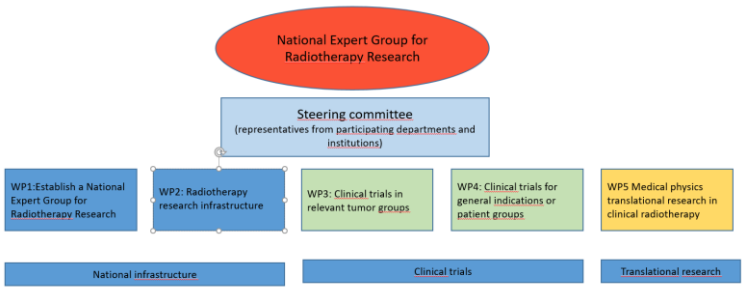


Figure 2

This figure shows the organization of the National expert group in radiotherapy research including the WPs and their main topics.



Activities and infrastructure including website, meetings, workshops and data distribution/sharing are described under WP1 and WP2.

International collaboration is important in radiotherapy research, and they are mentioned under Methodological approach and project plan.

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