

Imaging

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Chikako Suzuki

Per Grybäck

Lennart Blomqvist

Chikako.Suzuki@ki.se

Personalised Cancer Medicine Program

Karolinska Institutet

Science for Life Laboratory

Tomtebodavägen 23A

171 65 Solna, Sweden

Office phone: +46-704-54 02 74

info@pcm.ki.se

www.pcm-ki.se



**Karolinska
Institutet**

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Summary

The aim of this report is to highlight the current status of and challenges for “imaging” group related issues in relation to the Personalized Cancer Medicine (PCM) program at Karolinska Institutet (KI) as well as Karolinska University Hospital (KS, NKS).

For the PCM program, there are several major aspects related to imaging, 1. Oncological Imaging for diagnosis and for monitoring tumor response to the treatment, 2. Biopsy and Minimal Interventional Treatment, 3. Clinical Trial Imaging, 4. Experimental and Innovative Imaging and 5. Standardized Archiving and Reporting (Figure 1).

Among them, the Biopsy and Minimal Interventional Treatment is expected to play a critically important role in PCM for various analyses, for clinical decision support, for biomarker driven treatments, for biobanking and radiogenomics in the future (1-7). However, in the current situation we should admit that the capacity of Biopsy and Minimal Interventional Treatment has limitations due to shortage of dedicated radiologists/interventionists and dedicated facilities in NKS.

Other aspects have already been partly established in the department of diagnostic radiology, nuclear medicine and experimental research & imaging unit (KERIC). However, some changes are required in order to accommodate PCM. One example is increased collaboration with other PCM research groups.

PCM and Imaging

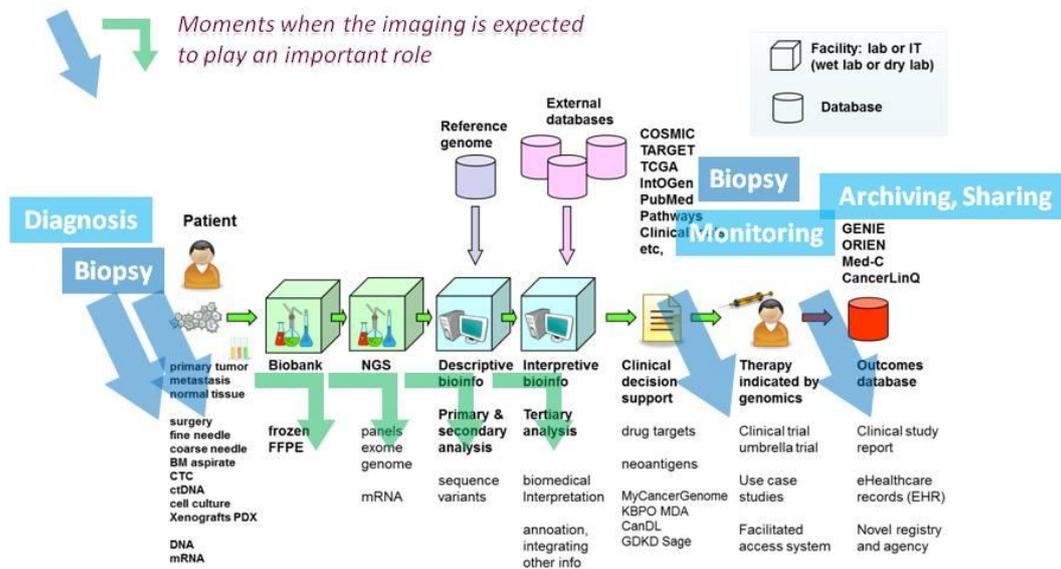


Figure 1. Moments when the imaging is expected to play a role in relation to PCM. (original figure from Personalized Cancer Medicine Program at Karolinska Institutet “Omics & Bioinformatics” by Anders Wennborg)

Clinical Imaging

Current status

Current Imaging Department at Karolinska University Hospital, Department of Imaging and Physiology consists of, in relation to oncology, Clinical CT, MR Imaging unit, Ultrasound unit, Interventional unit and Clinical Trial unit. Cutting-edge machines are equipped and many examinations are carried out daily. There are four multi-detector computed tomography (MDCTs) machines, one 3 tesla (T) - magnet resonance imaging camera (MR) and two 1.5 T-MRs, four ultrasound machines, all of them are capable for the “fusion-biopsy”, and three angio-/intervention theaters.

More than 30 multidisciplinary rounds per week, with various cancer cases are carried out every day.

The number of radiologists is more than 50, among them two professors, three assistant professors, 4 senior research fellows and 12 PhD students. However, in terms of cancer imaging, the number of dedicated radiologists is limited and most of them have been highly specialized in “organ” based malignancies, for example lung cancer, hepatic cancer, gastrointestinal cancer etc., and few have been specialized in general oncology regardless organs.

In the near future in NKS

CT

A total of eleven CT machines will be equipped in NKS. Three of them will be equipped close to each other in NKS, U1:3, plan 5. Among them, two CTs will be assigned both diagnostic use and high precision radiotherapy use. Both radiologists and oncologists will share the same space as well as CT machines, which may enable more detailed discussion among them and may contribute for precise delineation of tumor distribution, and radiation dose planning at the same time of diagnostic CT scan. This comprehensive CT usage might help to reduce unnecessary radiation dose as well as examination time.

MR

A total of twelve MR machines will be equipped in NKS. Two of them will be primarily for research purpose. Five of them will be 3 T (tesla), and the rest will be 1.5 T.

Additional one MR is planned for the new breast center, and will be dedicated for breast imaging.

PET-MR

In NKS, within the new research building (U2), one 3T PET-MR will be installed.

Radiologists for oncology

Many radiologists who are specialized in cancer imaging are expected to be employed in NKS. Radiology is becoming more organ subspecialized which also is reflected in the new Imaging Department of Imaging and Physiology Organization with organ based Functional Areas concerning radiology (thoracic, abdominal, trauma & musculoskeletal, neuro and pediatric radiology). The Functional Areas are divided in Functional Units (e.g. breast center, pelvic, pediatric oncology etc). The Functional Units work in close relationship with their clinical counterpart and this is thought to enhance patient flow and research in their field of operations. Considering clinical PCM research, where the number of umbrella and basket trials will increase and become major approaches, a broader collaboration setting is needed. Besides collaboration between functional units, more comprehensive educational program to enrich radiologists' knowledge outside her/his organ specialty are needed.

Molecular Imaging

Current status

Both Karolinska University Hospital Solna and Huddinge currently operate one clinical PET-CT each. The majority of examinations are clinical or related to clinical trial/research purposes. Due to lack of time and facility, the ability to conduct pure academic research examinations is hampered.

Karolinska Institutet, Department of Clinical Neuroscience, operates two PET cameras dedicated for brain/neurological studies. It is located near the Department of Neuroradiology. The majority of examinations are for human and animal (ape) research purposes, a few clinical brain/neurological studies are carried out as well.

Cyclotron: There is one cyclotron near the Department of Clinical Neuroscience in Karolinska University Hospital Solna with limited number of hot cells. It was originally dedicated for research purposes. However, to answer increasing demand for clinical PET examinations, it competes with isotope production and hot cell availability.

In the near Future in NKS

PET-CT

In NKS, three new PET-CTs will be equipped in the Department of Nuclear Medicine, which will be located close to the Radiotherapy Target Center. All of these will be equipped with gating and laser positioning systems for the precise Radiotherapy Targeting purposes.

Furthermore, one additional PET-CT is now planned for Karolinska Huddinge hospital in 2018, the total number of PET/CT:s will rise from 2 to 5.

PET-MR

Afore mentioned.

Cyclotron

In NKS, in the new research building (U2), two new cyclotrons will be installed. At the same building, the Radiochemistry Laboratory with more than thirty (30) hot cells will be facilitated.

Both of the new cyclotrons will be capable to produce traditional PET-isotopes as: Carbon-11 (^{11}C), Nitrogen-13 (^{13}N), Oxygen-15 (^{15}O), and Florine-18 (^{18}F). Besides them, Gallium-68 (^{68}Ga) and long lived radiometals as Zirconium-89 (^{89}Zr) will be available.

The new facility will have capacity to provide the hospital and KI with radiopharmaceuticals for clinic and research purposes.

Biopsy and Minimal Interventional Treatment Unit

Current Status

Good biopsy samples is one of the most important and indispensable components in modern clinical practice and PCM research (Figure 2)(8).

As the explosion of novel oncologic drugs, such as molecular targeted agents and immune therapies, the number of biopsy has been extremely increased in these couple of years.

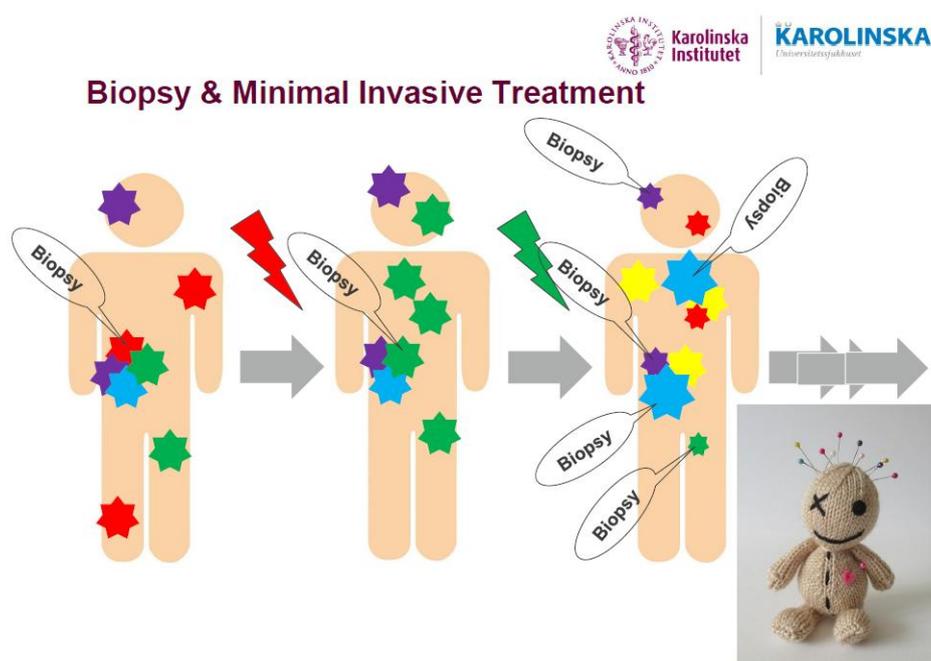


Figure 2. The increased knowledge of cancer biology with the detection of clonal evolution and heterogeneity results in greater needs for multiple tumor samples per patient.

In the Department of Diagnostic Radiology, there are four new ultrasound machines which are capable of precision biopsy and enable us to combine another imaging modality such as CT or MR with ultrasound real-time scanning image. Approximately four dedicated radiologists are capable of this cutting-edge technique as well as core needle biopsies.

For the CT-guided biopsies, one CT is dedicated for it and mainly two or three radiologists are dealing with that twice or three times per week.

MR-guided biopsy has just started in 2016 December.

In the near Future in NKS

In NKS, there are only four ultrasound dedicated examination rooms for both intervention and comprehensive health check purpose. There is no back up bed or ward for monitoring patient after biopsy or any other interventional procedures. One of the reasons is that, in NKS, Radiologist is expected to visit a patient, not vice versa, who is hospitalized with bringing the ultrasound machine and to perform bedside investigation. This will not meet the demands regarding safe and good quality multiple tumor biopsies needed for PCM

Clinical Trial Imaging Unit

Imaging plays a pivotal role to evaluate the efficacy of new anti-cancer medicine/ treatments.

Current status

In the new department of Imaging and Physiology, the final structure for clinical trial management is in process.

Current Clinical Trial Imaging Unit at Dept of Diagnostic Radiology Karolinska University Hospital Solna is dealing with more than 70 ongoing clinical trials and the majority of them are related to cancer treatments with both academic and commercial sponsors and many of them are phase II, III and a few phase IV (Figure 3).

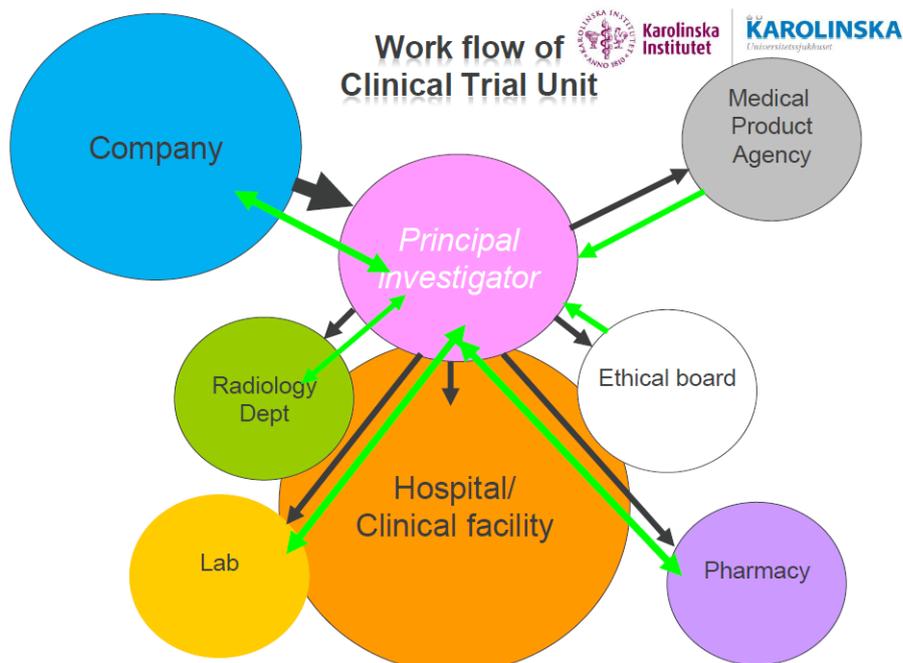


Figure 3. Current Work flow at Clinical Trial Imaging Unit, KS Solna

A clinical trial which requires monitoring with imaging, for example CT, MR and PET-CT, and/or tissue sampling or other interventions such as radiofrequency (RF) ablation is referred to the unit. Then radiology coordinators and coordinating nurses discuss the trial and allocate it to one dedicated radiologist who is asked to be responsible for the imaging part of the study (Figure 4).

Registration procedure or any other following procedures, such as sending images for the central review board and so on, is also organized by the unit.

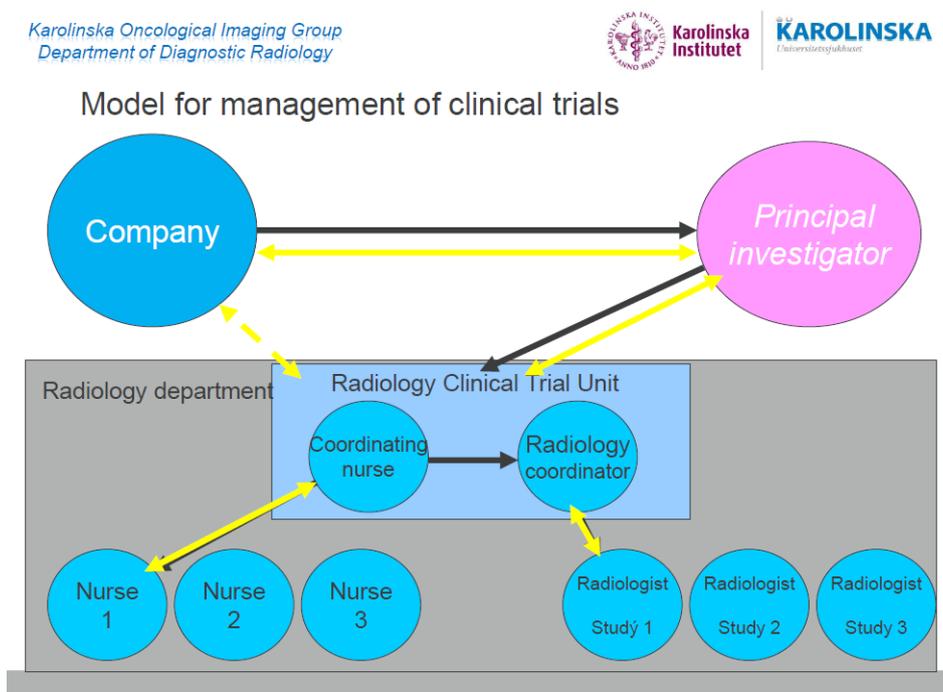


Figure 4. Workflow at the Clinical Trial Imaging Unit.

Challenges in regarding to PCM program

Current Clinical Trial Imaging Unit (Kliniska Prövnings Enheten) at Karolinska University Hospital Solna has been well functioning with a broad spectrum of clinical trials. However, most of the trials are investigating new therapies.

In the new imaging organization at Karolinska where an new department of Imaging and Physiology is established containing not only radiology but also Nuclear

Medicine, Clinical Physiology, Clinical Neurophysiology, Radiopharmacy and Radiation Physics. In this new Department, the radiological clinical trial unit is going to expand covering the entire imaging fields as well as creating a separate section with an oncological imaging unit for clinical studies.

Standardized Archiving and Communication System

Current Status

Department of Diagnostic Radiology has implemented the picture archiving and communication system (PACS) from 2004. All patient images produced at the Diagnostic Radiology at KS are converted into digital imaging and communications in medicine (DICOM) format, which is the international standard for medical images and related information (ISO 12052). Theoretically, DICOM files can be exchanged in different institutions both domestically and internationally. In fact, many images from other hospitals than KS are imported either as DVD or via on-line and many patient images obtained at KS are exported in the same ways.

In Sweden, a new multicenter network, called ALASSCA, has been established for colorectal cancer patients. Where major colorectal cancer centers and institutions are connected both in terms of academic research institutions and clinical routine care units (Figure 5).

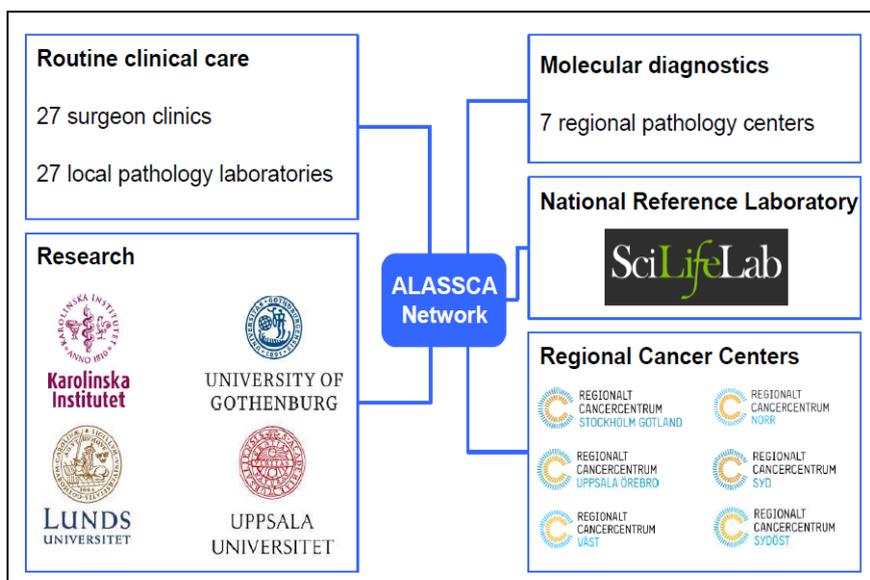


Figure 5. The ALASSCA network.

In the Near Future

For the region of Stockholm/Gotland, all radiology departments will during 2017 be connected to a common platform for archiving radiological images (Bild och Funktionstjänsten) provided by SECTRA. Since 2016 most department except Karolinska have already started storing images in this platform. This creates conditions for improved sharing of examinations and discussions, that will widen the knowledge within all hospitals in the region and facilitate research that need large amounts of imaging data that can also be used together with information from national health registries.

Proposal for a PCM oriented Cancer imaging Unit

As mentioned above, the current Department of Diagnostic Radiology covers a broad spectrum of oncological diseases and deals with various clinical trials from early to late phase. Regarding networks, a broadly spread network system, the ALASSCA network, which connects major domestic cancer institutions both clinical and laboratory, has already been established.

Four cores: Oncological Imaging & Biopsy, Clinical Trial, Experimental & Innovative Imaging and Network are, except for Biopsy, are quite well established and could be considered capable for answering the demands from PCM .

However, each unit have rather small dedicated groups with relatively weak connections to each other. For example, the Experimental Imaging Unit and Neurological Imaging Unit have quite little/limited connection to the Diagnostic Imaging unit. Furthermore, the connection or communication with KI or Sci-Life Lab is little or none.

To establish better cooperation, it is indispensable to build flexible and wide collaboration networks with representatives from the different units, in KI and SciLifeLab. For that purpose, we would like to propose the establishment of a dedicated Oncological Imaging Unit where all cancer imaging modalities and radiologists could come together and connect with the radiation oncology unit, the experimental imaging unit and the neurological imaging unit. Furthermore to develop the Clinical Trial Imaging Unit into a HUB which could communicate with KI and Sci-Life Lab in a coordinated and efficient way. For example, if a researcher would like to start a clinical trial/innovative research work, the Clinical Trial Imaging Unit would facilitate contact with the most suitable radiologist or imaging methods.

Challenges and Suggested actions for the PCM program

- To facilitate the establishment of a Biopsy and Minimal Interventional Treatment Unit.
- Implement educational programs to train radiologists in frontline PCM research.
- Contribute to the development of networks promoting PCM imaging research projects.

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