Recent advances in high precision radiotherapy resulted from significant advances in all three areas of importance to radiotherapy:

- **Target localization** (image registration, image segmentation, multimodality fusion, virtual simulation)
- **Treatment planning** (inverse treatment planning)
- **Dose delivery** (IMRT, TomoTherapy, CyberKnife)

In the near future, molecular imaging will allow determination of intra-tumoral volumes that require treatment with extra high doses as a result of:

- Tumor hypoxia
- Low intrinsic radiosensitivity
- Higher tumor clonogen density

This type of treatment will result in inhomogeneous target dose distributions which can only be precisely delivered with modern IMRT techniques and accurately delivered with volumetric imaging.
Significant improvements in target localization and treatment planning resulted in smaller planning target volumes (PTVs), yet the accuracy of the actual dose delivery is still limited by the uncertainty in target position at the time of treatment as a result of:

- Inter-fraction target movement (Between treatment fractions)
- Intra-fraction target movement (Within treatment fraction)
  - Breathing motion

Imaging of patient anatomy on the treatment machine just prior to each daily dose fraction provides an accurate knowledge of the target location on a daily basis and helps with the daily patient set-up on the therapy machine.

This technique is known as the image guided radiotherapy (IGRT) and has the potential of ensuring that the relative positions of the target volume and some reference marker for each fractional treatment are the same as in the treatment plan.

IGRT is characterized by the following features:
- Allows reduced treatment margins in the PTV
- Results in fewer treatment complications
  - Better normal tissue sparing
- Allows prescribed dose escalation
  - Reduced volume of normal tissue irradiated to high doses
- Reduces the chance of geographical miss of the target

Ideal IGRT system will:
- Allow the acquisition of soft tissue images at the time of each fraction of radiotherapy
- Have the ability to deliver a conformal dose distributions through an IMRT technique
- Be able to acquire 3D images
**Image Guided Radiotherapy**

- IGRT systems currently commercially available are based on direct integration of:
  - Kilovoltage or megavoltage imaging system and an isocentric linac (cone beam CT)
  - CT scanner and an isocentric linac
  - Megavoltage computerized tomography (MVCT) and linac mounted on a CT-type gantry
  - 3-D ultrasound system and an isocentric linac
  - On-line imaging with paired orthogonal planar imagers and a miniature linac mounted on a robotic arm

**Cone Beam Computed Tomography (CBCT)**

- CBCT imaging enables visualization of the exact tumor location just prior to patient treatment on a linac.
- CBCT integrates CT imaging with an isocentric linac and involves an acquisition of multiple planar images about the patient in the treatment position on the linac table.

**Cone Beam Computed Tomography**

- In CBCT, a filtered back-projection algorithm, similar to CT scanning algorithms, is used to reconstruct the volumetric images of:
  - Target volume
  - Sensitive structures
  - Landmarks in the patient or markers on patient’s skin.
- The volumetric data are then compared with the planning CT data and the associated optimized dose distribution, and the patient position is fine tuned to account for:
  - Tumor volume motion
  - Set-up error
Cone Beam Computed Tomography

- CBCT system integrated with an isocentric linac and based on kilovoltage x-ray beams consist of:
  - Conventional x-ray tube mounted on a retractable arm at 90° to the high energy treatment beam
  - Flat panel x-ray detector mounted on a retractable arm opposite to the x-ray tube
- In addition to cone beam images, the x-ray system can also produce radiographic and fluoroscopic images.

Cone Beam Computed Tomography

- CBCT images can also be produced with megavoltage x-ray beams (MVCT) produced with isocentric linacs
- The advantage of megavoltage CBCT is that no additional equipment is required for producing the cone beam since:
  - Beams come from the linac beam line
  - MVCT systems use the detector panel that is already installed on the linac for use in electronic portal imaging
- The disadvantage of MVCT systems is that, in comparison with KVCT systems, the MVCT systems produce an inferior tissue contrast

kV-CBCT Systems

Elekta, Stockholm, Sweden
Varian, Palo Alto, CA, USA
Computed Tomography Primatom

- Comprised of a linac and CT unit at opposite ends of a standard treatment table and is marketed by Siemens
- The main features of the system are:
  - The system allows precise CT imaging of patient anatomy prior to each fraction of radiotherapy
  - The patient can be shifted to compensate for target motion and set-up inaccuracies
  - The system allows clinicians to account for changes in target volume size and shape over a multifraction course of radiotherapy treatment

TomoTherapy

- The helical tomotherapy concept for delivering image guided radiotherapy was developed by T.R. Mackie and colleagues at the University of Wisconsin in Madison.
- The commercial TomoTherapy HI-ART system was released for clinical use and it combines the following features in one system:
  - Treatment planning
  - Patient positioning
  - Dose delivery verification
TomoTherapy

• In the tomotherapy system, the IMRT is delivered with a 6 MV X-band miniature linac mounted on a CT type gantry ring, allowing the linac to rotate around the patient.

• Beam collimation is accomplished with a computer controlled MLC that is also mounted on the gantry and has two sets of interlaced leaves that rapidly move in and out of the beam to constantly modulate the intensity of the radiation beam as the linac rotates around the patient.

During treatment, the table advances the patient through the gantry bore so that the radiation beam dose is delivered in a helical geometry around the target volume.

• The system is designed to obtain an MVCT scan of the patient anatomy before dose delivery.

• The MVCT image data are acquired with a 760 element Xenon ionization chamber array that rotates on the gantry opposite the linac.
TomoTherapy

• The MVCT-based image guidance allows fine adjustment of the patient’s position at every fraction to ensure that the dose is delivered precisely to the target volume
• A CT scan can also be taken immediately after a fraction of therapy with the patient still in the treatment position, allowing an evaluation of the true dose distribution delivered to the patient—Dose Reconstruction

Volumetric MVCT

TomoTherapy
The B-Mode Acquisition and Targeting (BAT) system is based on 2-D ultrasound images acquired prior to dose delivery. The images are used to realign the patient into the appropriate position on the treatment table.

The system consists of a cart-based ultrasound unit positioned next to a linac treatment table and is used by the radiotherapist to image the target volume prior to each fraction of radiotherapy treatment.

The relationship of the target volume to a reference point, usually the linac isocenters, is determined interactively by the user and compared with the target volume originally contoured in the CT data set.

Recommendations for required patient translation to move the target volume into the same position relative to the isocenters as in the treatment plan are made by the system and the patient is moved, based on this information, to gain better treatment accuracy.

The BAT system has found its widest application in pelvic radiotherapy, particularly in treatment of prostate cancer, since the prostate can move significantly from one day to another within the pelvis relative to bony anatomy.

Imaging the prostate target volume trans-abdominally with an ultrasonic probe on a daily basis and fine tuning the patient position based on system recommendation permits an accurate delivery of conformal treatment plans and allows target dose escalation without undo increase in bladder and rectal complications.
**BAT System**

- Images of a patient with prostatic adenocarcinoma captured by BAT®:
  - BAT allows the determination of the degree of organ movement that has taken place since the original CT treatment planning scan (top image).
  - The patient is repositioned accordingly (bottom image).
  - In this case, the patient was moved 0.1 cm to the left, 0.6 cm down, and 0.9 cm away from the linac.

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**ExacTrac Ultrasonic and X-ray Modules**

- Tumor positioning conventionally relies on external skin markers that are subject to inter-fraction shifts compromising the accuracy of dose delivery.
- Exactrac by BrainLAB is designed to address precise patient positioning by providing imaging of the target area around the tumor.
- X-ray images are taken just before treatment and the ExacTrac system automatically compensates for any patient misalignment.

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**Novalis**
**ExacTrac Ultrasonic**

- The ultrasound-based ExacTrac system can be used with any ultrasound unit and is comprised of a reflective marker array attached to an ultrasound probe. The marker array is calibrated by the ExacTrac infrared tracking system relative to reflective markers attached to patient’s body.
- The system works similarly to the BAT system and allows fine adjustment of the patient’s position to compensate for target motion and set-up inaccuracies.

**ExacTrac X-ray Modules**

- The ExacTrac x-ray imaging module provides high-resolution imaging of internal structures and organs
- During the positioning process the system calculates the discrepancy between the actual and the planned target position and compensates for any discrepancies with automatic treatment table motions
- Allows tracking of markers during treatment to compensate for intra-fraction motion

**CyberKnife**

- The CyberKnife was developed in the mid 1990s as an innovative tool for intracranial stereotactic radiosurgery.
- The dose is delivered with a miniature X-band (10^4 MHz) linac mounted on an industrial robotic arm in a combination that:
  - Offers excellent spatial accuracy in dose delivery
  - Allows, in comparison with isocentric linacs and tomotherapy machines, a great deal of flexibility in directing the beam toward the target
CyberKnife

Main components:
- 6 MV linac
- Robotic arm
- Treatment couch
- Imaging system

CyberKnife

• The CyberKnife radiosurgery system provides an innovative approach to image guided dose delivery that is based on:
  - On-line orthogonal pair of digital x-ray imagers
  - Patient axial CT data set possibly fused with MR and PET images
  - Miniature 6 MV X-band linac
  - Industrial robotic arm
• This new approach to highly accurate intracranial as well as extracranial delivery of high radiation doses with small radiation fields opens the field of radiosurgery to exciting new IGRT techniques
CyberKnife

- Target localization is achieved through a family of axial CT images that serve as a base for the determination of a set of digitally-reconstructed radiograph (DRR) images.
- A set of paired orthogonal x ray imagers determines the location of the lesion in the room coordinate system and communicates these coordinates to the robotic arm, which adjusts the pointing of the linac beam to maintain alignment with the target.

Owing to its on-line target imaging and automatic adjustment of the radiation beam direction to compensate for target motion, the CyberKnife provides a frameless alternative to conventional radiosurgery.
- The rigid invasive stereotactic frame which is the essential component of standard stereotactic radiosurgical treatments used for:
  - Target localization
  - Treatment set-up
  - Patient immobilization during treatment is not required for treatment with the CyberKnife.
Advantages of the CyberKnife over standard stereotactic radiosurgery techniques (Gamma Knife or linac-based):
- Dispenses with the rigid stereotactic frame
- Provides veritable image guided radiotherapy
- Allows for fractionated treatment of intracranial malignant tumours
- Allows treatment of extracranial lesions relying on the skeleton to provide a reference frame
- Allows treatment of other organs such as lung and prostate using surgically implanted fiducial markers as a reference markers
- Offers possibility for on-line tracking of target motion, which results either from patient motion during treatment or from organ motion within the patient during treatment

New Capabilities with IGRT
- Adaptive Radiotherapy
- 4D Radiation Delivery
- Hypofractionated Treatments

Adaptive Radiotherapy
- A full implementation of image guided radiotherapy will lead to the concept of adaptive radiotherapy (ART)
- In ART, dose delivery for subsequent treatment fractions of a course of radiotherapy can be modified to compensate for inaccuracies in dose delivery that cannot be corrected simply by adjusting the patient’s positioning like in the IGRT
- The causes of these inaccuracies may include:
  - Tumor shrinkage during the course of treatment
  - Patient loss of weight during the course of treatment
  - Increased hypoxia during the course of treatment
4D Radiation Delivery

- Respiratory motion has a significant effect on the dose delivery to targets in the chest and upper abdominal cavities and to compensate for these effects relatively large margins are added to clinical tumor volumes
- Extra margin results in:
  - Compromises to prescribed tumor doses
  - Treatment plans that adversely affect treatment outcome
  - Increased incidence of radiation induced morbidity

The quest for ever increasing tumor doses (dose escalation) to increase the tumor control probability (TCP) and simultaneously minimize the normal tissue complication probability (NTCP) requires a move towards smaller margins combined with an increased need to deal effectively with organ motion during treatment

The next big challenge in IGRT comes from the natural and unavoidable organ motion during treatment

To account for natural organ motion 4-D imaging technology was developed

4-D imaging technology allows viewing of volumetric CT images changing over the fourth dimension: Time

Examples of 4-D dose delivery techniques:
- Respiratory gating system (RGS), a special accessory added to a linac to compensate automatically and instantly for the effects of respiratory movement on external beam radiotherapy to the chest and upper abdomen
Hypofractionated Treatments

- Stereotactic Body Radiotherapy (SBRT)
  - Large fractions (>10Gy) delivered in a single fraction
  - Highly conformal delivery techniques required
  - Accurate spatial location of target necessary
- Precise and accurate radiation delivery minimize normal tissue irradiation
- Better outcome for early stage cancers of lung and liver as compared to conventional fractionation schedules

Summary

- Precise 3D dose distributions (IMRT)
  - Conformal prescription doses
  - Sharp dose gradients
- Image guidance crucial
- Clinical outcome will depend on accuracy of delivery:
  - Miss target – recurrence
  - Hit normal tissue – radiation induced complication

Questions?