Geometric uncertainties
Objectives

- To discuss the various types of geometric uncertainties
- To illustrate the importance of reducing geometric uncertainties
- To incorporate geometric uncertainties in a margin recipe
- To give examples how to reduce CTV-PTV margins
• Uncertainties in the delineation of the target volume are difficult to quantify and depend on many factors including the quality of the image registration and the experience of the clinician.

• They are taken into account in the GTV-CTV margin and consist of a part due to the delineation of the visible part of the target volume (GTV), and another part due to the uncertainty in the knowledge of the microscopic tumour extension (CTV).

• Both aspects can be reduced by using well defined delineation protocols, and continuous training of the physician.

• Better consistency in the drawing of the GTV can be obtained by using multiple image modalities (CT, MR, PET, ...).

• Organ motion due to physiological processes (breathing, heart beat, rectal and bladder filling) has to be quantified by using imaging information at different time periods.

• It is taken into account in the CTV-PTV margin, which can be reduced by knowing the actual position of the CTV during treatment, e.g., by using markers or repeat CT scanning.

• Set-up uncertainties are due to the day-to-day variation in the position of the CTV. Set-up uncertainties are also taken into account in the CTV-PTV margin and can be reduced by in-room imaging. They depend on the use of immobilisation devices, the carefulness of working of the therapists, and the type of in-room imaging.

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<table>
<thead>
<tr>
<th>Source</th>
<th>Systematic uncertainties</th>
<th>Random uncertainties</th>
<th>To be reduced by using:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delineation</td>
<td>1-?? mm</td>
<td>-</td>
<td>• Multiple imaging modalities&lt;br&gt;• Delineation protocols</td>
</tr>
<tr>
<td>Organ motion</td>
<td>&lt;1-50 mm</td>
<td>&lt;1-50mm</td>
<td>• Markers&lt;br&gt;• Repeat CT</td>
</tr>
<tr>
<td>Setup</td>
<td>1-5 mm</td>
<td>1-5 mm</td>
<td>• In-room imaging</td>
</tr>
</tbody>
</table>
Influence of margins on volume

Given the volume of a sphere:

\[ V = \frac{4}{3}\pi r^3 \]

Reduction of the CTV-PTV margin from 2.0 tot 0.5 cm around a spherical CTV with a diameter of 5.0 cm results in a decrease of the volume of the irradiated surrounding healthy tissue from 316 cm\(^3\) to:

a) 48 cm\(^3\)  
b) 96 cm\(^3\)  
c) 125 cm\(^3\)  
d) 225 cm\(^3\)  


- This exercise illustrates the volume of healthy tissue that can be spared by reducing the margin
- If the margin is large (the peel of the orange is thick), then the volume of healthy tissue that is irradiated (the volume of the peel) is almost as big as the CTV (the edible part of the orange)
Influence of margins on volume

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c) \(125 \text{ cm}^3\)

d) \(225 \text{ cm}^3\)


• How many of the participants had the right answer?
Geometric uncertainties (errors)

• Small errors add up; large errors may occur when a number of small errors are in the same direction

• Errors that are made once per patient:
  • Systematic errors
  • Stochastic (determined by probability) for a group of patients
  • Standard deviation of systematic errors: $\Sigma$

• Errors that are made during each treatment fraction:
  • Random errors
  • Standard deviation of random errors: $\sigma$

Random errors are those that are evaluated by statistical methods and systematic errors are those that are evaluated by other means.

The standard deviation of the systematic and random errors of a group of patients is given by the Greek symbol $\Sigma$ (capital sigma) and $\sigma$ (small sigma), respectively.

• This figure shows random and systematic setup deviations for a group of five patients, both in individual patients and in population-based data.

• The standard deviation of all systematic and all random setup errors of the whole group (population) of patients can be combined according to a “margin recipe”.
Random setup errors will yield the correct dose at the centre of the field, but will cause a blurring of the cumulative dose distribution at the border of the field.

A systematic setup error will shift the cumulative dose distribution, and may cause an under-dosage of part of the target volume and an over-dosage of healthy tissue.

Random setup errors can be corrected by measuring the patient position just before treatment (i.e., online), while systematic setup errors can be corrected just before treatment that day (online), or using an offline protocol and correcting the position before the next treatment fraction.
• It should be noted that when using a CTV-PTV margin recipe, there still is a finite chance that some patients of a population of “identical” patients have a microscopic extension outside this margin.
• For instance, the CTV of a non-small cell lung tumour might be the GTV expanded by an isotropic margin of 9 mm if one wishes to treat 90% of that patient group correctly. However, a margin of 12 mm might be necessary if one wishes to cover all patients.

CTV to PTV margin

Margin recipe to cover the CTV for 90% of the patients within the 95% isodose surface

\[
\text{PTV margin} = 2.0 \Sigma + 0.7 \sigma \\
\text{PTV margin} = 2.5 \Sigma + 0.7 \sigma
\]

(Sstrom et al., 1999)  
(van Herk et al., 2000)

\[\Sigma = \text{SD of all systematics errors combined quadratically}\]

\[\sigma = \text{SD of all random errors combined quadratically}\]
In this example of a patient with bladder cancer we will show the importance of reducing the geometric uncertainty with respect to the size of the CTV-PTV margin.
Bladder

Partial bladder irradiation

• 30 fractions / 2.25 Gy or 25 fractions / 2.4 Gy

• Full bladder instruction

• Very difficult to treat with high geometrical accuracy
  – Bladder filling changes within and between fractions
  – Tumour may change in shape

• Therefore: large margins are needed
  – 2 - 4 cm depending on what area of the bladder is irradiated

Online strategy is needed

• Bladder tumour patients have an uncontrolled random day-to-day change in CTV position and shape due to the large variation in bladder filling

• Only online verification of the tumour position will allow the use of small margins.
• According to this margin recipe example, a huge CTV-PTV margin (green area) is required for the treatment of bladder tumours of patients having a full bladder.
A large CTV-PTV margin will result in a large dose in organs at risk and will limit the dose that can be given to the PTV.

• If the position of the tumour can be measured just before the treatment, then a small field can be directed to the correct position of the tumour during that particular day (treatment-of-the-day).
• By measuring the day-to-day variation in the position of the tumour, the systematic and random uncertainty in that position can be determined.

• Averaging these data for several patients will allow the assessment of the margin for a group of bladder cancer patients.

\[
\sigma = \text{Day-to-day deviation from average (SD)} \\
\Delta = \text{Systematic error, the difference between treatment average and planning CT} \\
\Sigma = \text{Patient population variability of } \Delta \text{ (SD)}
\]

Margin = 2.5 \cdot \Sigma + 0.7 \cdot \sigma
• At the start of the treatment the population based margin can be used, which can be reduced if more information is available from CT scans about the systematic and random error in the setup of this particular patient.
How to reduce the margin?

Margin = 2.5 $\sum$ + 0.7 $\sigma$

First focus on SYSTEMATIC errors, i.e. collect as much data as possible in the preparation and initial treatment phase:

- Use good tools and protocols to reduce the delineation uncertainty
- Average multiple CT scans to estimate and correct for the mean position of the moving organ
- Use in-room imaging to measure and correct the average set-up error

To implement such an approach you need correction protocols

- A portal imaging procedure using an electronic portal imaging device (EPID)
- The images on the screen at the right bottom are a portal image (left) with bony anatomy (in green) projected on a digitally reconstructed radiograph (right) to indicate possible setup errors.
This example illustrates the reduction of setup errors of prostate cancer treatments by using portal imaging.
The frequency of systematic setup errors varies for different treatment sites, and can be reduced considerably by using in-room imaging techniques.
Reducing margins

“Technical” margins can be reduced by measuring and improving daily setup with in-room imaging tools such as:

- 2-D/3-D systems (e.g., EPIDs, CBCT, ultrasound)
- external fiducials (e.g., ExacTrac®)
- internal fiducials (e.g., Calypso®)

• A number of in-room imaging systems have been developed to improve daily set-up reproducibility, as will be elucidated in more detail in presentation 20
• They all aim at the same goal: to daily reproduce as closely as possible the position of the patient and the internal organs and structures during the initial planning imaging session (usually determined with CT)
• The better the reproducibility, the smaller the PTV. The limit would be a perfect repositioning with a CTV-PTV margin = 0 for setup uncertainties
• There would however remain a margin to be added for respiratory movements or organ filling variation (CTV-ITV margin)
• But even these physiological variations can be, at least partially, accounted for
• For example, the use of a rectal balloon in prostate cancer treatment avoids the daily variations in volume of the rectum
The various in-room imaging systems that are used for measuring setup errors are discussed in presentation 20: “Treatment verification: imaging and dosimetry”

How to reduce the CTV-PTV margin?

Setup error data measured at AZ-VUB, Brussels, Belgium, using various in-room imaging methods

Fig. 1. An estimate of the distribution (AZ-VUB) of set-up errors for prostate treatments resulting from positioning with respectively skin markers and room-laser alignment, infrared tracking, automated fusion between DRR and actual X-ray images, and matching of implanted markers. The systematic error is calculated as the standard deviation of the mean deviation of individual patients. The random error is defined as the standard deviation of the individual deviations of all patients after subtraction of the corresponding mean.

(D. Verellen. Chapter 9 in: Image-guided IMRT)

• In this figure four methods of measuring setup errors during prostate cancer treatment are compared.
How to reduce the CTV-PTV margin?

(Derived from the data at AZ-VUB provided by Verellen)

<table>
<thead>
<tr>
<th>Method</th>
<th>Systematic, $\Sigma$ (1 SD, mm)</th>
<th>Random, $\sigma$ (1 SD, mm)</th>
<th>Margin (mm) $2.5\Sigma + 0.7\sigma$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conventional</td>
<td>7.7</td>
<td>9.2</td>
<td>25.7</td>
</tr>
<tr>
<td>IR</td>
<td>4.8</td>
<td>5.2</td>
<td>15.6</td>
</tr>
<tr>
<td>DRR</td>
<td>2.8</td>
<td>5.0</td>
<td>10.5</td>
</tr>
<tr>
<td>Markers</td>
<td>2.6</td>
<td>2.6</td>
<td>8.3</td>
</tr>
</tbody>
</table>

In this table the systematic and random setup errors, measured during prostate cancer treatment using the four methods shown in the previous slide, were used to calculate a CTV-PTV margin.
Motion management and use of 4-D images

- Movement or anatomical changes in the patient can be visualized by using a time-series (four-dimensional) representation.

This slide shows the effect of a systematic and random error on the position of a moving CTV (orange oval) with respect to the PTV derived from the planning CT (dotted blue line).
• By adjusting the average position, the systematic error in the position of the 4-D PTV can be removed.

• The random error cannot be removed and will result in a 4-D PTV that is larger than the PTV obtained from a 3-D planning CT scan.
• When using small fields for the treatment of lung tumors, there exists a risk of missing the target volume
• On the other hand, when using large fields, extensive damage to normal tissue may occur
• By means of advanced irradiation techniques small fields can still be used in a safe way by taking tumour position changes due to breathing during treatment into account

Motion management and use of 4-D images

- Movement or anatomical changes in the patient can be visualized by using a time-series (four-dimensional) representation.
- For instance, daily-repeated or respiration-correlated (cone-beam) CT scans allows visualization of time-dependent changes in morphology.
Respiration-correlated 4-D CT scanning

- Raw CT data sorting based on breathing signal: both 4-D CT and 4-D CBCT scans
- Select from 4-D CT the single 3-D scan with the tumour in the time-averaged position: mid-ventilation CT → into TPS
- Verify mid-ventilation position with 4-D CBCT scan

• This slide illustrates the use of 4-D cone-beam CT (CBCT) to verify the tumour position just before treatment.
During a series of fractions of radiotherapy of lung tumours, a number of anatomical changes in the patient may occur, requiring specific planning and treatment strategies.
Four-dimensional radiotherapy accounts for anatomic motion by characterising the motion, creating a treatment plan that accounts for this motion, and verifying the motion just before or during treatment.
The choice of the CTV-PTV margin requires expertise from oncologists, physicists and radiotherapy technologists (radiographers); it's TEAM WORK!

Talk to each other and discuss all (difficult) cases.
The GTV-CTV margin is needed to take microscopic tumour spread into account.

Knowledge of microscopic tumour extension is generally based on careful analysis of surgical specimen, and (by definition) not on imaging techniques.

Uncertainties regarding the GTV-CTV margin can therefore only be reduced by gathering more surgical data.

An example of the choice of the GTV-CTV margin for head-and-neck cancer can be found in: Grégoire et al., CT-based delineation of lymph node levels and related CTVs in the node-negative neck: DAHANCA, EORTC, GORTEC, NCIC, RTOG consensus guidelines. Radiother Oncol 69, 227-236, 2003.
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