SBRT: management of respiratory motion
Lung mobility

4D CT for target definition

IGRT

Tumor and MLC tracking

SBRT vs standard RT in lung

Not only breathing motion

Take home messages
Influence of organ motion

The North American Experience with Stereotactic Body Radiation Therapy in Non-small Cell Lung Cancer

Robert D. Timmerman, MD,* Clint Park, MD,* and Brian D. Kavanagh, MD, MPH†

FIGURE 2. Uncontrolled tumor motion requires enlargement of a beam’s eye view radiation portal to avoid target inaccuracy. Careful assessment and control of motion dramatically decrease normal tissue exposure.
Influence of organ motion in thorax

Sonke IJROBP 2008

Korreman BJR 2015

Dieleman et al. IJROBP 2007
SBRT efficiency

Past

Now

Future

Slotman, ESTRO 2011
Rationale for motion management

Highly conformal radiation techniques (SBRT):

- high precision
- risk for geographical miss

Control for:
- Patient set-up errors
- Organ motion
- Patient movement
Lung mobility

4D CT for target definition

IGRT

Tumor and MLC tracking

SBRT vs standard RT in lung

Not only breathing motion

Take home messages
4D SBRT

2005-2010

4D CT for Target definition

2011-2013

CBCT as IGRT

2012-now

4D CBCT Target tracking MLC online

PubMed.gov
US National Library of Medicine National Institutes of Health

Search results
Items: 1 to 20 of 112

Search results
Items: 1 to 20 of 88
Target definition expansion

- Gross Tumor Volume (GTV)
- Biological Target Volume (BTV)
- Clinical Target Volume (CTV)
- Internal Target Volume (ITV)
- Setup Margin (SM)

Espansione per la micromalattia
Movimento del tumore
Margini di posizionamento
4D-CT

(x,y,z,time)
Semiautomatic technique for defining the internal gross tumor volume of lung tumors close to liver/spleen cupola by 4D-CT

Pietro Mancosu
Department of Radiotherapy, IRCCS Istituto Clinico Humanitas, Rozzano, 20089 Milano, Italy

Semiautomatic method to identify the best phase for gated RT in lung region by 4D-PET/CT acquisitions

Pietro Mancosu
Department of Radiotherapy, IRCCS Istituto Clinico Humanitas, Rozzano, 20089 Milano, Italy

Contrast enhanced 4D-CT imaging for target volume definition in pancreatic ductal adenocarcinoma

Pietro Mancosu, Valentino Bettinardi, Paolo Passoni, Simone Gusmini

4D-PET data sorting into different number of phases: a NEMA IQ phantom study

Pietro Mancosu, Roberto Sghedoni, Valentino Bettinardi
How to evaluate the breathing motion
4D CT reconstruction

Scanning position

I

II

III

time

4D-TC images (Cine)

Breathing curve

Phases

4D-TC

Phase 1

Phase 6
4D CT reconstruction
4D CT reconstruction

Mancosu Med Phys 2012
4D TC - CONTORNAMENTO
Free breathing CT
4D CT - lung
Gating
4D SBRT

2005-2010

4D CT for Target definition

Search results
Items: 1 to 20 of 112

2011-2013

CBCT as IGRT

Search results
Items: 1 to 20 of 88

2012-now

4D CBCT
Target tracking
MLC online
Tools for verifying patient position and adapting treatment plans. Monitoring during beam on time

Reduction of PTV margins
Reduction of irradiated volume
Image Guided RadioTherapy
CLINICAL INVESTIGATION

IMAGE-GUIDED RADIOThERAPY VIA DAILY ONLINE CONE-BEAM CT
SUBSTANTIALLY REDUCES MARGIN REQUIREMENTS FOR
STEREOTACTIC LUNG RADIOTHERAPY

GTV position pre-correction: Planning CT GTV in Red; Pre-Correction GTV in Green.

Transverse  |  Sagittal  |  Coronal

GTV position post-correction: Planning CT GTV in Red; Post-Correction GTV in Blue.

Transverse  |  Sagittal  |  Coronal

308 CBCT, 24 pts

Tumor positional errors using stereotactic body frame coordinates for setup:
NO IGRT 10-12mm,
YES IGRT <2 mm.

Fig. 1. Precorrection and postcorrection cone-beam CT (CBCT) images for an example protocol patient treated in the stereotactic body frame. (Top) Gross tumor volume (GTV) position precorrection: planning CT GTV in red; precorrection GTV in green. (Bottom) GTV position postcorrection: planning CT GTV in red; postcorrection GTV in blue.
IGRT: how much?

Modern radiotherapy using image guidance for unresectable non-small cell lung cancer can improve outcomes in patients treated with chemoradiation therapy

Matthew P. Deek¹, Sinae Kim², Ning Yue¹, Rekha Baby¹, Inaya Ahmed¹, Wei Zou¹, John Langenfeld³, Joseph Aisner⁴, Salma K. Jabbour¹

Overall survival
With number of subjects at risk

+ Censored
Logrank P=0.0139

Weekly based imaging

Daily based imaging

JTD 2016
Times are changing fast
Humanitas experience

Volumetric modulated arc therapy with flattening filter free (FFF) beams for stereotactic body radiation therapy (SBRT) in patients with medically inoperable early stage non small cell lung cancer (NSCLC)

Pierina Navarria\textsuperscript{a,*}, Anna Maria Ascolese\textsuperscript{a}, Pietro Mancosu\textsuperscript{a}, Filippo Alongi\textsuperscript{a}, Elena Clerici\textsuperscript{a}, Angelo Tozzi\textsuperscript{a}, Cristina Iftode\textsuperscript{a}, Giacomo Reggiori\textsuperscript{a}, Stefano Tomatis\textsuperscript{a}, Maurizio Infante\textsuperscript{b}, Marco Alloisio\textsuperscript{b}, Alberto Testori\textsuperscript{b}, Antonella Fogliata\textsuperscript{c}, Luca Cozzi\textsuperscript{c}, Emanuela Morenghi\textsuperscript{a}, Marta Scorsetti\textsuperscript{a}

3DCRT:
Simulation: FB CT
IGRT: MV 2D-2D daily
Delivery: 6MV

VMAT RA:
simulation :4DCT
IGRT: kV-CBCT daily
Delivery: 10FFF

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|}
\hline
 & 3DCRT & VMAT RA & $p$ \\
\hline
\textbf{Ipsilateral lung} & & & \\
$V_{5 Gy}$ [%] & 31.4 $\pm$ 11.9 [6.6–57.8] & 25.3 $\pm$ 11.8 [6.8–54.0] & 0.03 \\
$V_{10 Gy}$ [%] & 22.6 $\pm$ 9.9 [0.0–45.6] & 16.4 $\pm$ 8.9 [3.8–46.0] & 0.007 \\
$V_{20 Gy}$ [%] & 11.8 $\pm$ 7.0 [0.0–26.7] & 7.3 $\pm$ 4.9 [1.2–26.6] & 0.002 \\
MLD [Gy] & 7.2 $\pm$ 3.0 [0.9–12.6] & 4.9 $\pm$ 2.4 [1.2–13.3] & $<$0.001 \\
\hline
\textbf{Contralateral lung} & & & \\
$V_{5 Gy}$ [%] & 2.9 $\pm$ 4.8 [0.0–18.7] & 2.0 $\pm$ 3.0 [0.0–11.3] & 0.31 \\
$V_{10 Gy}$ [%] & 0.6 $\pm$ 2.5 [0.0–13.3] & 0.0 $\pm$ 0.2 [0.0–0.9] & 0.19 \\
$V_{20 Gy}$ [%] & 0.1 $\pm$ 0.6 [0.0–3.5] & 0.0 $\pm$ 0.0 [0.0–0.0] & 0.31 \\
MLD [Gy] & 0.8 $\pm$ 0.8 [0.1–3.5] & 1.0 $\pm$ 0.5 [0.1–2.6] & 0.38 \\
\hline
\end{tabular}
\caption{Control at 12 months}
\end{table}
4D SBRT

2005-2010
4D CT for Target definition

2011-2013
CBCT as IGRT

2012-now
4D CBCT Target tracking (LINAC-MRI)
Different techniques

**TRACKING**

**BREATH-HOLD**

**GATING**
Real-time Tracking of tumor

Calypso®

Clarity®
Online Fluoroscopy
Gating acquisition system

• Stereo View Video camera attached to room ceiling above couch
  – Track respiratory motion by measuring position of reflective markers

• Based on breathing pattern gates beam and imaging
  – Amplitude Based Gating
  – Phase Based Gating
  – Breath Hold
  – Patient Visual and Audio Couching

• Synchronised imaging 2D and fluoro during Delivery at given gate phases
Gating and 2D imaging
Gating during delivery: gamma evaluation

No gating

Gating 72 interruptions

10FFF
10Gy
2400MU/min
1 arc
Interplay effect

Experimentally studied dynamic dose interplay does not meaningfully affect target dose in VMAT SBRT lung treatments

Cassandra Stambaugh  
*Department of Physics, University of South Florida, Tampa, Florida 33612*

Benjamin E. Nelms  
*Canis Lupus LLC, Merrimac, Wisconsin 53561*

Thomas Dilling, Craig Stevens, Kujtim Latifi, Geoffrey Zhang, Eduardo Moros, and Vladimir Feygelman  
*Department of Radiation Oncology, Moffitt Cancer Center, Tampa, Florida 33612*

2013
Gating and SBRT

End expiration: Beam on

End inspiration: Beam off

NSCLC Stage I; prescription: 20Gy x 3 days
2465+2682 MU, Total BOT: 320s
Treatment phase: 50%-75%

Complete response after 2 months
• Analyze tumor motion
• Verify tumor size
Dynamic tumor tracking using the Elekta Agility MLC

Martin F. Fast,  Simeon Nill,  James L. Bedford,  Uwe Oelfke

The authors have developed a new control software which interfaces to the Agility MLC to dynamically program the movement of individual leaves, the dynamic leaf guides (DLGs), and the Y collimators (“jaws”) based on the actual target trajectory. A motion platform was used to perform dynamic tracking experiments with sinusoidal trajectories. The actual target positions reported by the motion platform at 20, 30, or 40 Hz were used as shift vectors for the MLC in beams-eye-view. The system latency of the MLC (i.e., the average latency comprising target device reporting latencies and MLC adjustment latency) and the geometric tracking accuracy were extracted from a sequence of MV portal images acquired during irradiation for the following treatment scenarios: leaf-only motion, jaw + leaf motion, and DLG + leaf motion.
Calypso

Mixed RadioFrequency/InfraRed localization/tracking system Transponder based
Calypso Real Time Tracking

Anchored Beacon® for Lung SABR

Beacon for Prostate SABR

Surface Beacon

Soft Tissue Beacon
Calypso

Mixed RadioFrequency/InfraRed localization/tracking system Transponder based
Calypso: Lung case with MLC tracking

First in man

The first patient treatment of electromagnetic-guided real time adaptive radiotherapy using MLC tracking for lung SABR

Jeremy T. Booth\textsuperscript{a,b,*}, Vincent Caillet\textsuperscript{a,b}, Nicholas Hardcastle\textsuperscript{a,c}, Ricky O’Brien\textsuperscript{b}, Kathryn Szymura\textsuperscript{a}, Charlene Crasta\textsuperscript{a}, Benjamin Harris\textsuperscript{a}, Carol Haddad\textsuperscript{a}, Thomas Eade\textsuperscript{a}, Paul J. Keall\textsuperscript{b}

\textsuperscript{a} Northern Sydney Cancer Centre, Level 1 Royal North Shore Hospital; \textsuperscript{b} University of Sydney, Schools of Physics or Medicine, Sydney; and \textsuperscript{c} Centre for Medical Radiation Physics, University of Wollongong, Wollongong, Australia
First in man

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\textsuperscript{a} Northern Sydney Cancer Centre, Level 1 Royal North Shore Hospital; \textsuperscript{b} University of Sydney, Schools of Physics or Medicine, Sydney; and \textsuperscript{c} Centre for Medical Radiation Physics, University of Wollongong, Wollongong, Australia
Lung mobility
4D CT for target definition
IGRT
Tumor and MLC tracking
SBRT vs standard RT in lung
Not only breathing motion
Take home messages
SBRT vs conventional fractionation

Phase III randomised trial

SPACE – A randomized study of SBRT vs conventional fractionated radiotherapy in medically inoperable stage I NSCLC

Jan Nyman a,*, Andreas Hallqvist a, Jo-Åsmund Lund b, Odd-Terje Brustugun c, Bengt Bergman a, Per Bergström d, Signe Friesland e, Rolf Lewensohn e, Erik Holmberg a, Ingmar Lax e

CT was performed before the first treatment to verify tumor reproducibility with predefined tolerance limits. CBCT (cone beam CT) and 4DCT was allowed but only available at a few sites. A heterogeneous dose distribution within the PTV was used. The prescribed

SBRT (3 fractions)

Tot: 45Gy (periphery) 66Gy (center)

Standard (35 fractions):

Tot: 70Gy
Stereotactic ablative radiotherapy versus standard radiotherapy in stage 1 non-small-cell lung cancer (TROG 09.02 CHISEL): a phase 3, open-label, randomised controlled trial

David Ball, G Tao Mai, Shalini Vinod, Scott Babington, Jeremy Ruben, Tomas Kron, Brent Chesson, Alan Herschtal, Marijana Vanevski, Angela Reza, Christine Elder, Marketa Skala, Andrew Wirth, Greg Wheeler, Adeline Lim, Mark Shaw, Penelope Schofield, Louis Irving, Benjamin Solomon, on behalf of the TROG 09.02 CHISEL investigators

Added value of this study

To our knowledge, this was the first randomised trial to compare stereotactic ablative body radiotherapy (SABR) with standard radiotherapy in patients who had pathologically proven non-small cell lung cancer at stage T1–T2aN0M0, as determined by $^{18}$F-fluorodeoxyglucose (FDG)-PET scanning. This was also, to our knowledge, the first trial in which all radiotherapy plans took into account tumour motion, either with 4D CT (for patients randomly assigned to SABR) or FDG-PET scanning (for patients randomly assigned to standard radiotherapy).
Lung mobility
4D CT for target definition
IGRT
Tumor and MLC tracking
SBRT vs standard RT in lung
Not only breathing motion
Take home messages
Target uncertainties in Radiotherapy

- Setup Error
  - patient positioning
  - out-of-plane rotation
  - weight loss
  - non-rigidity
  - skin mark shifts
  - tension
  - involuntary motion
  - bowel gas motion
  - respiration
  - peristalsis
  - cardiac motion

- Organ Motion
  - volume changes
  - deformation
  - bladder/rectum filling
  - intra-abdominal pressure

- Interfraction Variability
- Intrafraction Variability
Question of motion

CBCT pre

CBCT post
Cone beam CT pre- and post-daily treatment for assessing geometrical and dosimetric intrafraction variability during radiotherapy of prostate cancer

Giacomo Reggiori,† Pietro Mancosu,†a Angelo Tozzi,† Marie C Cantone,‡ Simona Castiglioni,† Paola Lattuada,† Francesca Lobefalo,† Luca Cozzi,§ Antonella Fogliata,§ Piera Navarria,† Marta Scorsetti†

Radiation Oncology Dept.,† IRCCS Istituto Clinico Humanitas, Milano (Rozzano), Italy; Physics Dept.,‡ Università degli studi di Milano, Milano, Italy; Medical Physics Unit,§ Oncology Institute of Southern Switzerland, Bellinzona, Switzerland

pietro.mancosu@humanitas.it

Prostate Intra-Motion

Prostate displacement

Fraction of displacements

Time (min)

> 3mm

> 5mm

4 × 10^5

6 × 10^7

8
Difficult case@Humanitas

35 Gy
7 Gy x 5 fr
RA, 10FFF
BoT: 108s
All objectives ok
Prostate with Calypso

Simulation CT

CBCT 1
### Localization Summary

<table>
<thead>
<tr>
<th>Isocenter Localization</th>
<th>Lat (Left+)</th>
<th>Long (Sup+)</th>
<th>Vert (Ant+)</th>
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</thead>
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<tr>
<td>Shift from Initial Setup (cm):</td>
<td>0.30</td>
<td>-0.02</td>
<td>-0.01</td>
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<tr>
<td>Time:</td>
<td>09:37:00 AM</td>
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<table>
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<tr>
<th>Intertransponder Distances</th>
<th>Planned</th>
<th>Measured</th>
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<td>A to B (cm):</td>
<td>3.18</td>
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<td>B to C (cm):</td>
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<td>C to A (cm):</td>
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<th>Geometry Checks</th>
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<td>Rotation - Pitch (°)</td>
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<td>Rotation - Roll (°)</td>
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<td>2</td>
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<tr>
<td>Rotation - Yaw (°)</td>
<td>30</td>
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<tr>
<th>Session Overrides</th>
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<tr>
<th>Tracking Summary</th>
<th>None</th>
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<table>
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<tr>
<th>Summary of Target Excursions Outside of Tracking Limits</th>
<th>Tracking Time while Radiation Detected: 0:01:40</th>
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<tbody>
<tr>
<td>Direction</td>
<td>Left</td>
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<tr>
<td>Time (sec)</td>
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<tr>
<td>Percent</td>
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<tr>
<td>Max Excursion (mm)</td>
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<th>Adaptive Couch Repositioning Request Summary</th>
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<table>
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<tr>
<th>Couch Angles Summary</th>
<th>Angles: Nominal Only (0°)</th>
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<table>
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<tr>
<th>Set Zero Summary</th>
<th>Approver</th>
<th>Time</th>
<th>ΔLat (Left+)</th>
<th>ΔLong (Sup+)</th>
<th>ΔVert (Ant+)</th>
<th>Lat (Left+)</th>
<th>Long (Sup+)</th>
<th>Vert (Ant+)</th>
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<td>AdvTherapist</td>
<td>09:45:30 AM</td>
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<td>AdvTherapist</td>
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<td>0.0 cm</td>
<td>0.1 cm</td>
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<td>-0.4 cm</td>
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<td>0.0 cm</td>
<td>0.0 cm</td>
<td>0.0 cm</td>
<td>-0.4 cm</td>
<td>0.1 cm</td>
<td></td>
</tr>
</tbody>
</table>

*This association was finalized and approved by AdvTherapist on Oct 1, 2014 09:37:11 AM*
Calypso: Patient tracking
Prostate with Calypso (after 1 min)
Calypso: Patient tracking
Difficult case@Humanitas

PSA - prostate specific antigen
10.5 ng/ml April 2014
1.4 ng/ml Jan 2015
1.2 ng/ml Jan 2017

35 Gy
7 Gy x 5 fr
RA,10FFF
BoT:108s
All objectives ok
Non-Difficult case @ Humanitas

38 Gy
9.5 Gy x 4 fr
RA, 10FFF
BoT: 108s
All objectives ok
Calypso: Patient tracking

Patient Session Report
Tracking

Session: Jan 25, 2017 10:00 AM
Reported: Jan 26, 2017 03:22 PM

Simulation CT

CBCT

Set Zero
Gating Status: Enabled
Calypso: Patient tracking

Patient Session Report
Tracking

Session: Jan 25, 2017 10:00 AM
Reported: Jan 26, 2017 03:22 PM

L-R

C-C

A-P

CBCT

Set Zero

Gating Status: Enabled

No Radiation Data Available
How to limit the motion

Eccles et al, Int J Rad Onc Biol Phys 2010
PHYSICS CONTRIBUTION

FOUR-DIMENSIONAL COMPUTED TOMOGRAPHY SCAN ANALYSIS OF TUMOR AND ORGAN MOTION AT VARYING LEVELS OF ABDOMINAL COMPRESSION DURING STEREOTACTIC TREATMENT OF LUNG AND LIVER

JOHN H. HEINZERLING, M.D.,* JOHN F. ANDERSON, B.S.,* LECH PAPIEZ, PH.D.,* THOMAS BOIKE, M.D.,* STANLEY CHIEN, PH.D.,† GEOFFREY ZHANG, PH.D.,* RAMZI ABDULRAHMAN, M.D.,* AND ROBERT TIMMERMAN, M.D.*

Fig. 2. Tumor motion at varying levels of abdominal compression.
Take home messages

• Lung (but not only) have motion induced by breathing

• Many technologies are available for monitoring:
  Before/During treatment

• Imaging

• Imaging

• Imaging

• Imaging
Questions?

Monte Rosa, 4664 m - Italy

pietro.mancosu@humanitas.it