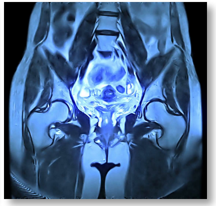
(Imaging Based) Respiratory Gating

Advanced Motion Compensation in Modern Radiotherapy

Dinu Purice
Supervisor: Prof. Marco Riboldi

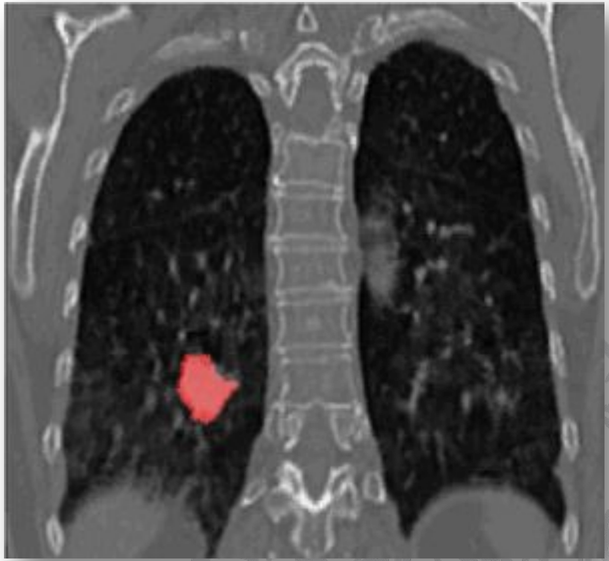




Contents

Introduction and Overview

Tumour movements:

- Inter-fractionary motion (~1-2 days)
  - caused by weight-loss or physiological changes, positioning mismatch
  - most relevant in head & neck cancer cases
- Intra-fractionary motion (~minutes)
  - caused by respiration, peristaltic motion, seldomly heartbeat
  - most relevant in thoracic and abdominal cases



Introduction and Overview

Gating compensation strategy:

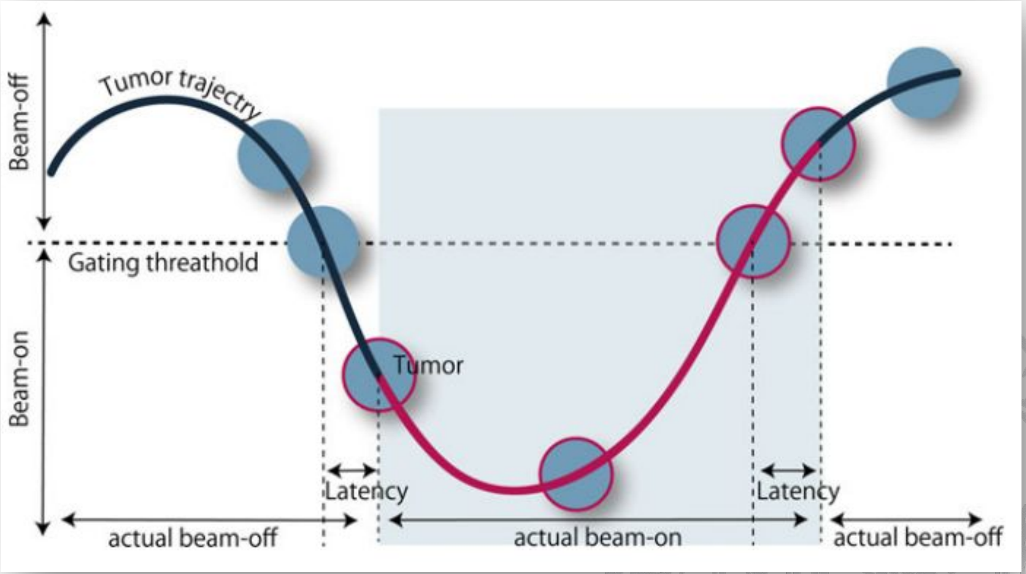
- Introduce gating with beam-on and beam-off stages based on gating signal
- Irradiate during breathing cycle part with least tumour motion (end-exhalation) or maximum lung volume (end-inhalation)
- Find trade-off between residual motion and duty cycle

Introduction and Overview

Gating method advantages:
- maximizes dose conformity
- minimizes normal tissue dose delivery (OARs, healthy tissue)

Resulting challenges:
- latency-induced delay
- radiation pulse synchronization
- longer treatment time (respiration drift)

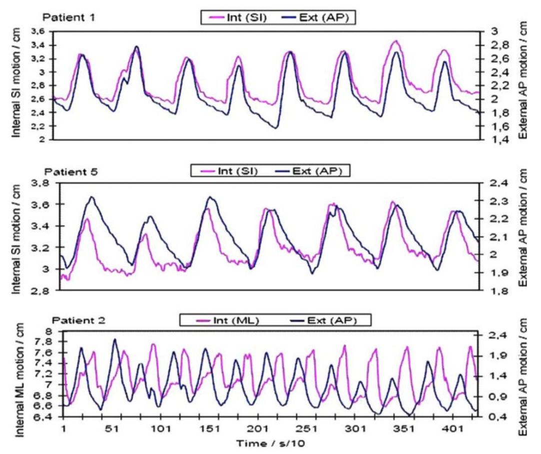
Compatible with other strategies
- deep-inspiration breath hold (DIBH)
- active breathing-control (ABC)
- abdominal compression



Introduction and Overview

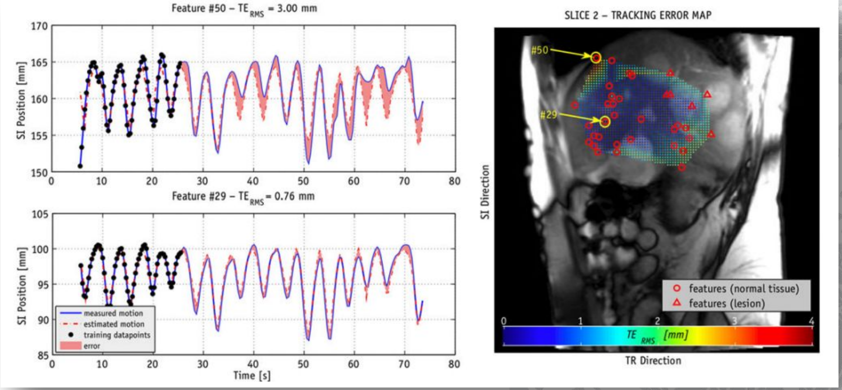
External gating signal

- respiratory-correlated imaging (e.g. 4d-CT with markers + infrared cameras)
  - requires good correlation between marker and tumour motion
  - non-invasive, easy to implement



Internal gating signal

- tracking using fiducial markers, other radio-opaque materials
- trackerless options:
  - fluoroscopic imaging
  - ultrasound
  - MRI



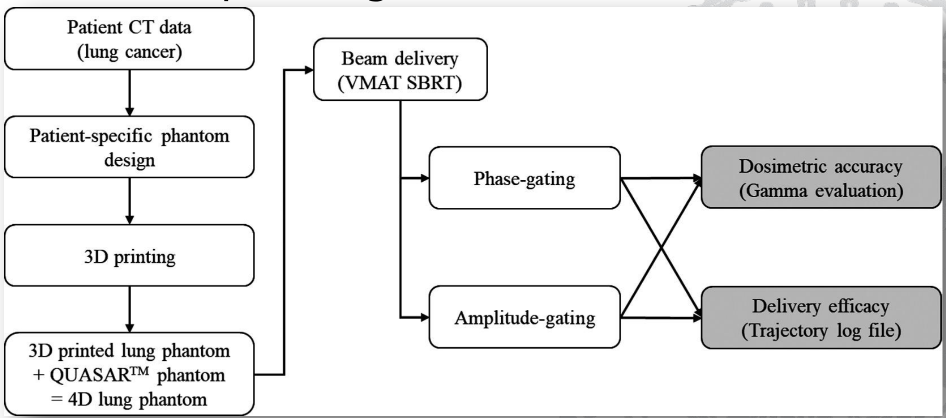
Introduction and Overview

Phase based gating

- percentage level of respiratory cycle
- vulnerable to interfractional position variation
- only accounts for respiratory motion

Displacement (amplitude) based gating

- within a specific position defined during treatment planning
- internal tracking necessary
- can be expanded to account for peristaltic motion



Contents

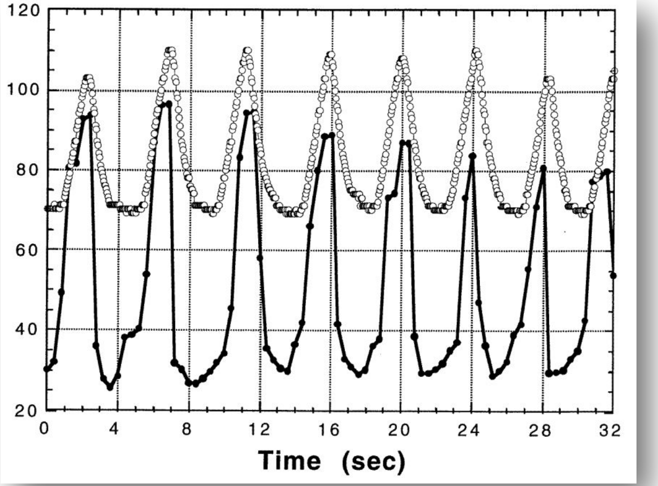
Historical Pioneering

“Respiration gated radiotherapy treatment: a technical study” [Kubo96]

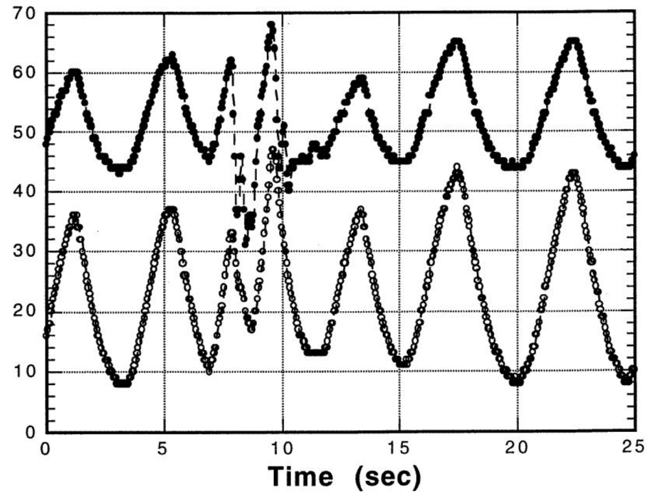
- At the time respiratory gating techniques in development (since 80s) medically used in very few institutions
- Aspects investigated:
  - Optimal respiration monitoring
  - Organ displacement measuring
  - Linear accelerator gating
    - Varian 2100C, discontinued in 2007
- Respiration monitoring through:
  - Strain Gauge (SG): thoracic movements
  - Temperature Sensors (TS, thermistor and thermocouple): exhaled/inhaled air temp.
  - Pneumotachograph (PT): exhaled/inhaled air volume

Historical Pioneering

- Respiration monitoring outcome:
  - all methods adequately reproduce breathing
  - gradual TS rises and steeper falls reflect slower inhalation than exhalation
  - TS requires less adjustments (same room and lung temps.)
  - SG and TS advantageous in terms of comfort for the patient



SG + TS vs SG + PT



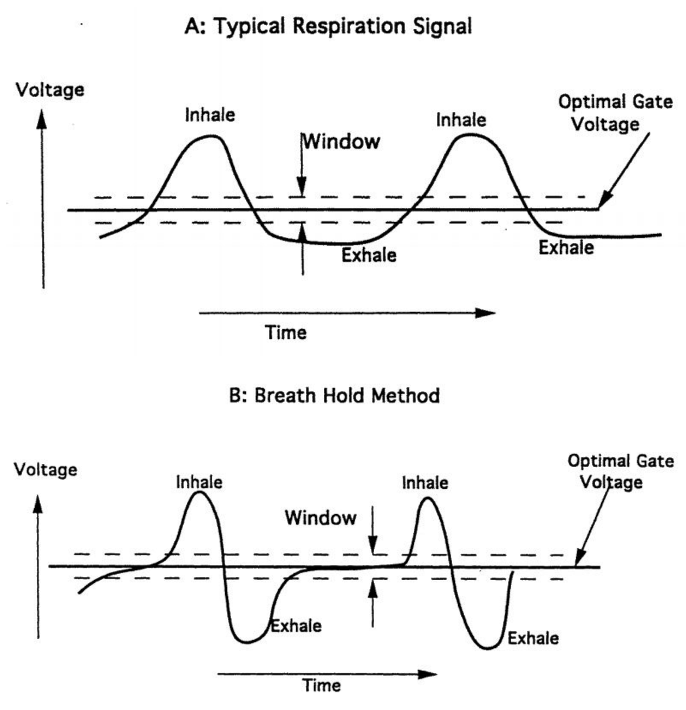
Historical Pioneering

- Organ motion recorded on fluoroscopic X-ray images 30 images/second

- Lung:
  - 15-20 mm diaphragm superior/inferior movement
  - 5-7 mm lateral chest wall movement
  - radio-opaque dummy seeds displacements: 15 mm at tip, 5 mm at 15 cm upstream linearly in-between

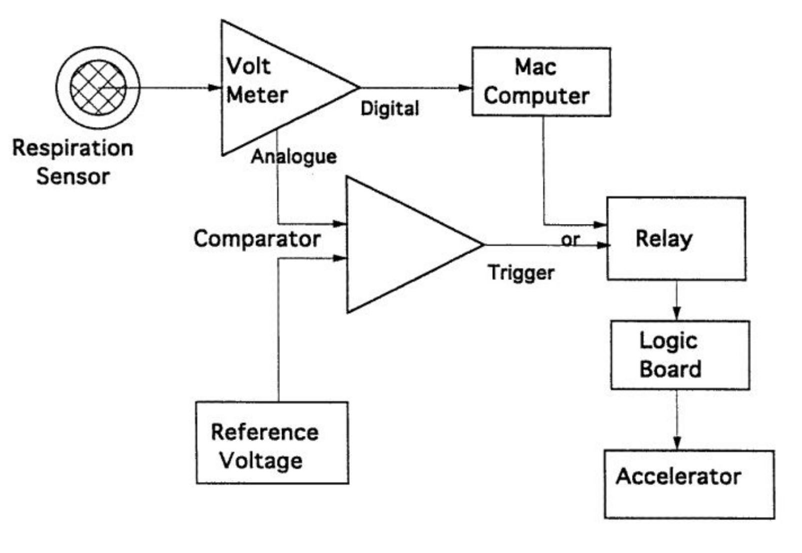
- Breast
  - 7 mm outward movement
  - larger amount of lung interacts with the beam in outward position

- In both cases breath hold methods provide significantly longer duty cycle



Historical Pioneering

- Accelerator gating tested in phantom study
  - beam characteristics unaltered
  - less than 0.1 % difference in absorbed dose gated vs non-gated tests
  - 1.1 % and 0.6 % symmetry change inplane and crossplane
  - 1.2 % and 0.7 % uniformity change inplane and crossplane



"When other potential treatment inaccuracies, such as patient positioning errors and inaccurate treatment volume description are reduced, the usefulness of a respiration gated technique may be more appreciated"

Contents

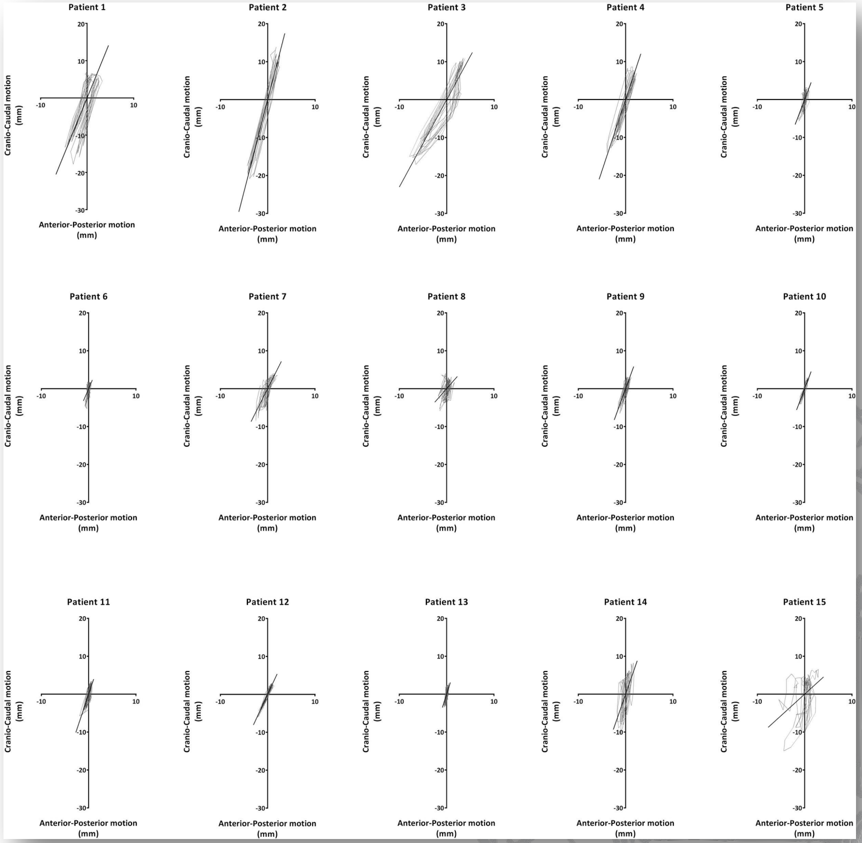
The motion to compensate

"MRI-based tumor motion characterization and gating schemes for radiation therapy of pancreatic cancer" [Heerkens14]

- Pancreatic cancer, aggressive, low survival rate
- OARs: duodenum, stomach
- Data: two cine MRI of 60s, 15 patients
  1.5 Tesla scanner, 16 channel phased array
- ROI visually tracked using inferior and superior points
  (inferior point visually illustrated)
  Motion quantified via Minimum Output Sum of Squared Error
- Palliative surgery performed so no pathology validation available

The motion to compensate

- Tumour motion averages:
  - 15 mm in craniocaudal direction (6-34 mm, sd 9 mm)
  - 5 mm in anteroposterior direction (1-13 mm, sd 3 mm)
  - 3 mm lateral direction (2-5 mm, sd 1 mm)
  - 0.4 mm between superior and inferior edges
- Small lateral movements allow 2D emphasis
- High variability between patients requires individual approach
- Common practice: active motion management for motion > 8 mm



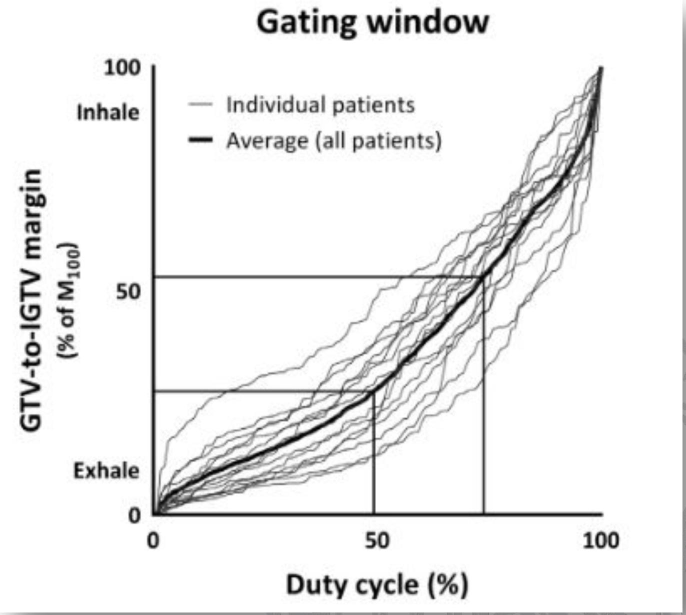
The motion to compensate

- Gating strategy:
  - End expiration position (EEP) more reproducible:
    sd of 0.8 mm vs 1.9 mm for end inspiration pos (EIP)
  - 70 % of the time tumour closer to EEP than EIP
    (49-85 % sd 9 %)

- IGTV - union of all GTVs integrated over the beam-on time

- Aiming for lower margin:
  higher dose conformity; lower OARs dose
  BUT
  longer treatment time, risk of drift motion errors

- Full target coverage obtained with margin of ¼ of breathing amplitude at 50 % duty cycle
  (however large inter-patient variation)

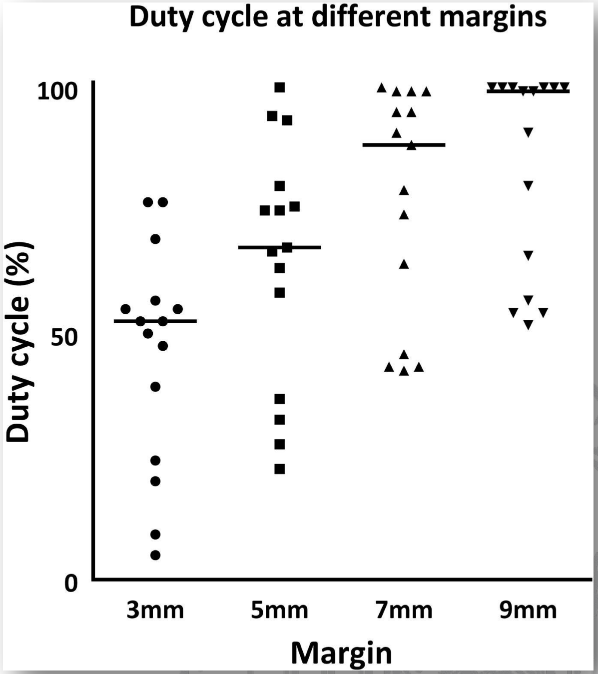


The motion to compensate

- 5 mm margin sufficient for 11/15 patients at 50 % duty cycle
- 3 mm margin for 11/15 patients at 25 % duty cycle

- EEP suboptimal for 4/11 patients
  - instability of EEP hinders its definition
  - duty cycles become too short for fixed margins
  - midvent gating might be an option

- Always a good idea: reduce tumour motion through abdominal compression (at best no further motion management needed, at worst increased duty cycle)



Contents

Gating strategies and their effectiveness

“Comparing the effectiveness and efficiency of various gating approaches for PBS proton therapy of pancreatic cancer using 4d-MRI datasets” [Dolde19]

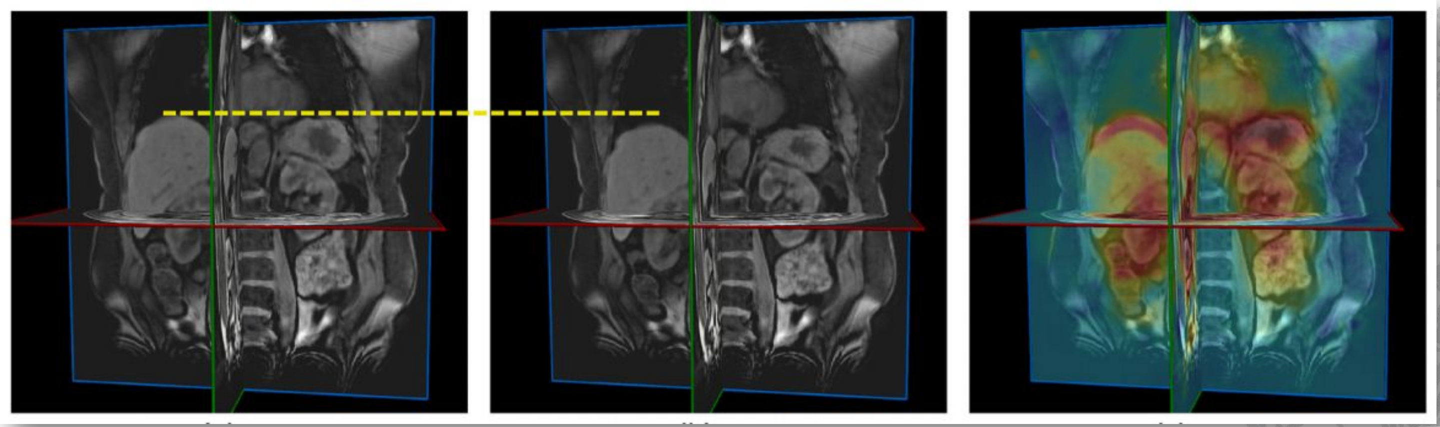
- Effectiveness of gating in normal tissue sparing largely investigated but no variation in gating strategies

- Various gating strategies investigated depending on CTV motion

- Find most suitable strategy in terms of
  - effectiveness (low interplay effect)
    - interplay more critical in proton vs photon!
    - evaluated by dose homogeneity index HI=d5/d95
  - efficiency (high duty cycles)

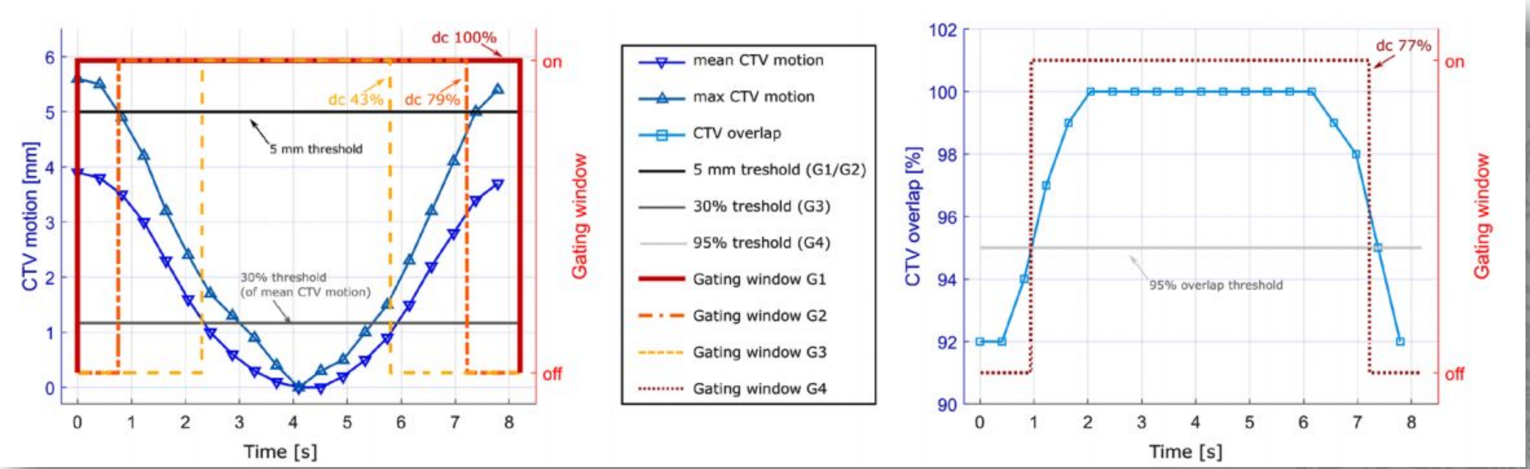
Gating strategies and their effectiveness

- 8 pancreatic cancer patients
  up to 6 repeated 4d-MRI scans per patient
  3d treatment planning CT and 4d-CT used for the planning phase
- CTV delineated, ITV based on phases of 4d-CT scan, 3mm extension
- 4d-MRI acquired on 1.5 T MR scanner (Magnetom Aera, Siemens)
- Abdominal compression desired, but often impossible



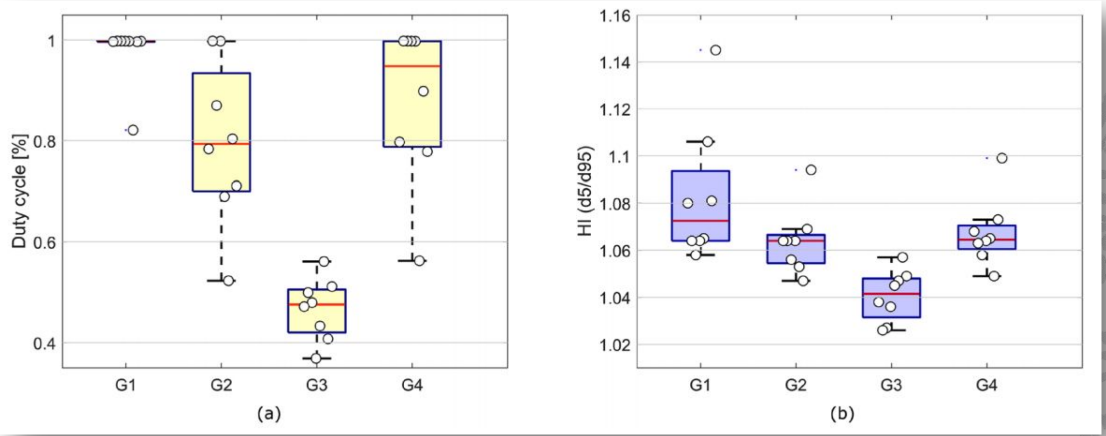
Gating strategies and their effectiveness

- G1: mean CTV motion amplitude (relative to EE breathing phase) < 5 mm
- G2: maximum CTV motion amplitude (relative to EE breathing phase) < 5 mm
- G3: mean CTV motion amplitude (relative to EE breathing phase) < 30 % of the mean CTV motion amplitude in EI breathing phase
- G4: overlap between current phase CTV and EE phase CTV > 95 %



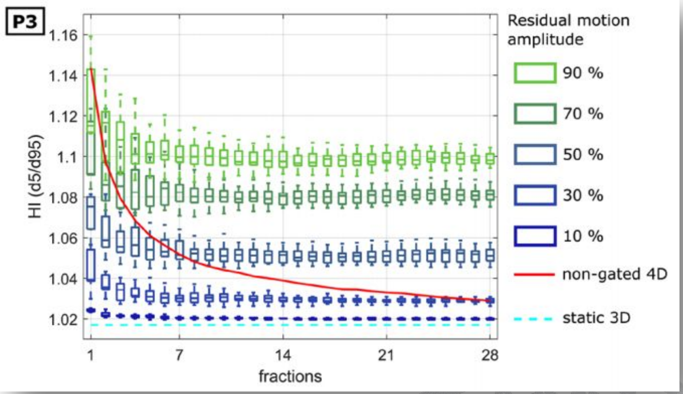
Gating strategies and their effectiveness

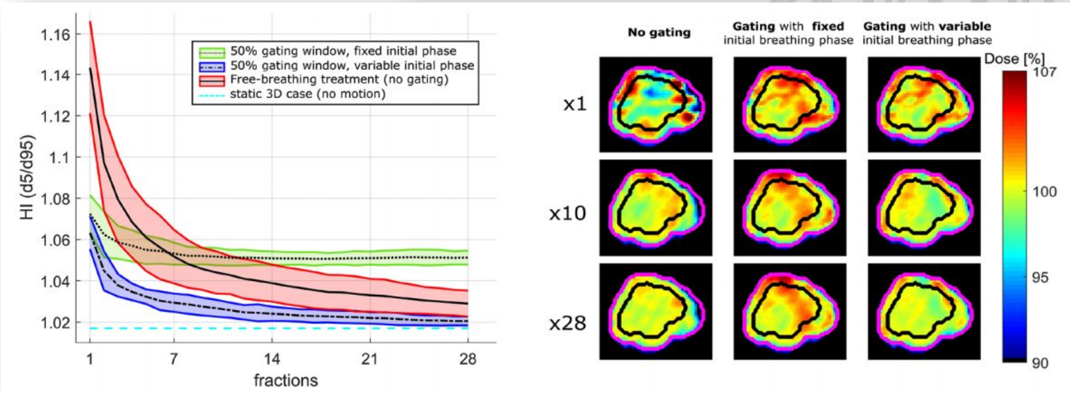
- Mean CTV motion of 2-8 mm observed with max 15 mm; breathing cycles 3-10 s
- G1 unhelpful as no gating for most patients
- G3 lowest duty cycle (≈30 %) followed ascendingly by G2, G4
- G3 best HI (although small difference between G2, G3, G4)



Gating strategies and their effectiveness

- Statistically, interplay effect mitigated in free breathing case
- Gating results in lower mitigation due to fixed threshold criteria
- After many fractions, HI lower for non-gated approach
- G3 consistently maintains better mitigation
- Variable initial phase shown to further mitigate interplay





Gating strategies and their effectiveness

- G3 found to be most favourable, preferably with variable initial phase

- Investigations on image-based gating criteria, assuming 3d time-resolved real-time MRI
  - not generally available for clinical use
  - MR-LINAC shows an important step in this direction
    G4 already in use for MR-LINAC treatments

- while 4d-MRI too computationally intensive for online imaging
  - pancreatic motion can be restricted to 2d plane
  - deep learning based methods potentially usable to reduce imaging and reconstruction time, keeping high MRI quality

Contents

Current context of the method

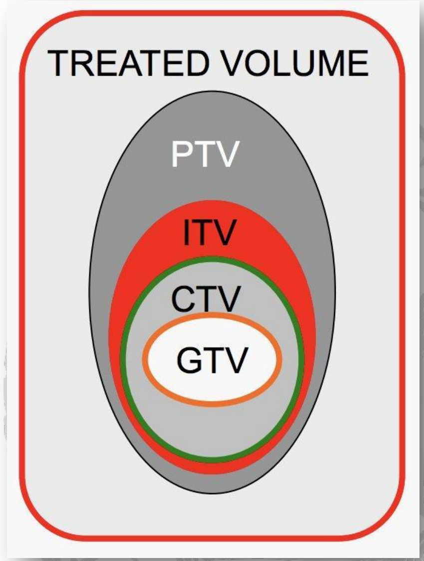
“Stereotactic Body Radiotherapy for Hepatocellular Carcinoma: A Dosimetric Comparison Study Focused on the Impact of Respiratory Motion Managements”

[Yoon16]

- Dosimetric assessment between CyberKnife (CK) tumour tracking and respiratory-gated volumetric-modulated arc therapy (VMAT)

- Based on 29 liver cancer cases:
  - treated with VMAT; 4d-CT gated over 30-70 % phase
  - each compared to two CK plans, based on
    - CK1: original PTV (with ITV)
    - CK2: modified PTV (without ITV)

- Performance evaluated in terms of:
  - conformity index
  - PTV coverage
  - OARs dosage and normal tissue sparing



Current context of the method

- Overview of the investigated problem:
  - tumour motion of up to 3 cm
  - breath-holding techniques not suitable for - 40 % cases
  - abdominal compression reduces motion by only about 2.3 mm
  - respiratory gating used s.t. margin reduced to within 5 mm
  - note: CK adds the option of continuous tracking

- Compared treatment deliveries:
  VMAT: gantry rotation, dose rate modulation, continuous multi-leaf collimator (MLC) with respiratory gating
  vs
  non-isocentric robot-based CK Synchrony system with real-time tumour tracking (bypassing the ITV margin)

Treatment delivery systems	
isocentric	non-isocentric
MLC	cone-type collimator
respiratory gating	tumour tracking

Current context of the method

- Clinical goals:
  - total dose of 45 Gy in 3 fractions
  - prescription dose to cover >95 % of PTV
    conformity index < 1.2
  - OAR constraints

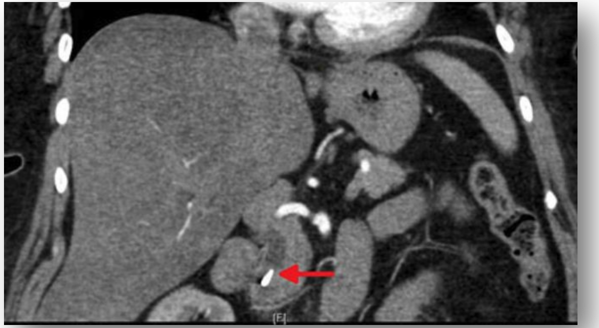
Organ at Risk	Constraints
Normal Liver	$V_{d<15Gy} > 700$ cc
Normal Liver	$D_{mean} < 13$ Gy
Esophagus	$D_{2cc} < 21$ Gy
Large bowel	$D_{2cc} < 21$ Gy
Stomach	$D_{2cc} < 18$ Gy
Duodenum	$D_{2cc} < 18$ Gy
Spinal cord	$D_{max} < 18$ Gy

- Tumour motion:
  - average 14.5 ± 5.7 mm
  - (<10 mm) 8 cases
  - (11-20 mm) 17 cases
  - (20-30 mm) 4 cases

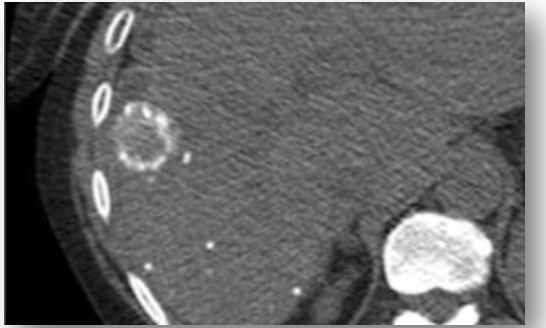
- Tumour motion reduced to 5.0 ± 2.3 mm with gating

Current context of the method

- Respiratory Gating:
  - Internal tracking:
    - 2 cases: surgical clips
    - 18 cases: compact iodized oil tracking (lipiodol)
    - 9 cases: three fiducial markers (gold seeds)
  - 4d-CT during normal breathing, each sorted into 10 CT series/respiration phase
  - GTV contoured at EE phase CT referencing enhanced contrast CT and/or MRI
  - Gating of 30-70 % of phase s.t. respiratory motion ≈ 5 mm



Surgical clip



Lipiodol

Fiducial markers

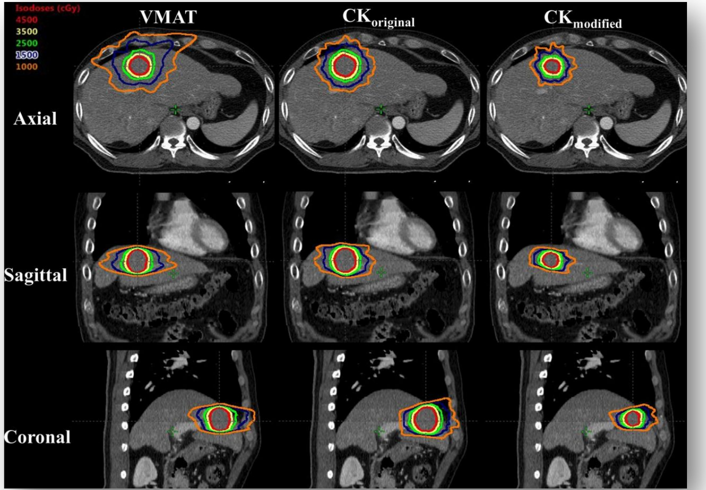
Current context of the method

- VMAT treatment procedure
  - PTV_VMAT = GTV + ΔITV + 5 mm
    - ITV = GTV + ΔITV accounts for tumour motion during beam-on
    - Enlargement by 5 mm margin accounts for uncertainties due to interfractional tumour motion; delineation uncertainties
  - PTV volume 27.1 ± 15.0 cc

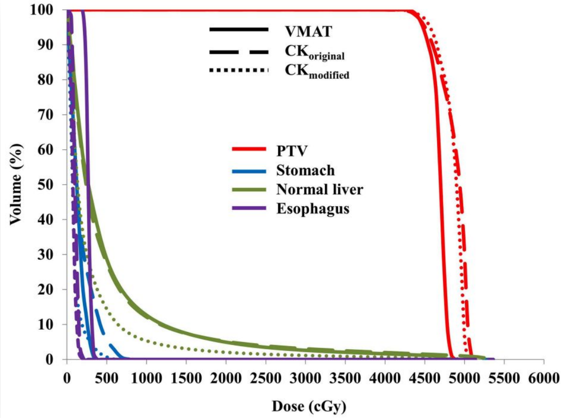
- CK treatment procedure
  - based on previously acquired data
  - CK1: PTV_CK1 = PTV_VMAT
  - CK2: PTV_CK2 = GTV_VMAT + 5 mm
    PTV volume reduced to 15.6 ± 5.0 cc

Current context of the method

- PTV volume:
  - VMAT: 24cc (9-65 cc)
  - CK2: 12 cc (5-41 cc)
- Conformity Index:
  - VMAT: 1.05
  - CK1, CK2: 1.17



- PTV coverage:
  - VMAT 93 %
  - CK1: 96.6 %
  - CK2: 96.9 %
- <u>CK2 normal tissue (>15 Gy) reduced:</u>
  - <u>by 1.75 to VMAT</u>
  - <u>by 1.61 to CK1</u>



Current context of the method

- Results somewhat at odds with [Paik15]:
  - **“Dosimetric comparison of volumetric modulated arc therapy with robotic sterotactic radiation therapy in hepatocellular carcinoma”**
  - reports CK better dose conformity, VMAT better normal tissue sparing and shorter sessions

- Area of conflict:
  - higher dose (60 Gy), weaker constraints
  - [Paik15] delineated GTV on slow CT
    GTV becomes ITV, used for both systems
  - [Paik15] compares delivery systems rather than full tracking AND delivery capacity

Beam delivery systems	
isocentric	non-isocentric
MLC	cone-type collimator
~~respiratory gating~~	~~tumour tracking~~

- Continuous tumour tracking proved more efficient than respiratory gating

Contents

Summary and Outlook

- Rather efficient and straightforward to implement
- Highly customizable (internal/external, phase/amplitude, gating strategy)
- Complements other motion management techniques
- Requires good tumour tracking
  - in turn enables real-time tumour tracking with continuous irradiation
- Significant research effort towards real time tracking
- Machine learning being introduced in internal trackerless methods

Summary and Outlook

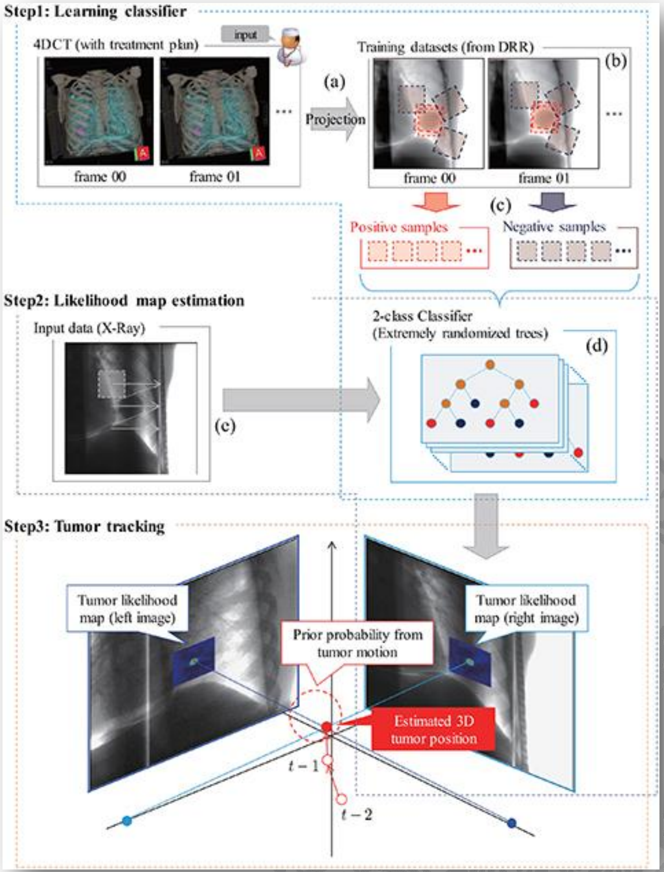
- Fluoroscopic imaging in the context of gating
  - essentially 2d array of pixel values
  - perfect for deep learning algorithms

“A machine learning-based real-time tumour tracking system for fluoroscopic gating of lung therapy”

[Sakata20]

- Tracking algorithm consists of:
  - learning classifier (DRR generated from 4dCT, optimized with ERT)
  - likelihood map estimation
  - tumour tracking

- Reported position tracking errors of 1.03 ± 0.34 mm



Publication prospecting

- Search engines:
  - Google, Google scholar
  - PubMed
- Keywords: respiratory gating, gated radiotherapy, ultrasound gated radiotherapy, MRI gated radiotherapy, fluoroscopic gated radiotherapy
- Additionally:
  - “citations” and “cited by”
  - journal impact factor check
  - number of citations (relative to the publication year)
  - publication year constraints:
    - no constraints for history
    - 2005-2020 for evaluations and comparisons
    - 2015-2020 for research direction

Literature and References

[Kubo96] Hideo D. Kubo et al "Respiration gated radiotherapy treatment: a technical study", *Physics in Medicine & Biology*, 1999

[Heerkens14] Hanne D. Heerkens et al. "MRI-based tumor motion characterisation and gating schemes for radiation therapy of pancreatic cancer", *Radiotherapy and Oncology,* 2014

[Dolde19] Kai Dolde et al. "Comparing the effectiveness and efficiency of various gating approaches for PBS proton therapy of pancreatic cancer using 4d-MRI datasets", *Physics in Medicine & Biology*, 2019

[Yoon16] KyongJun Yoon et al "Stereotactic Body Radiotherapy for Hepatocellular Carcinoma: A Dosimetric Comparison Study Focused on the Impact of Respiratory Motion Managements", *PLoS ONE*, 2016

[Paik15] Eun Kyung Paik et al "Dosimetric comparison of volumetric modulated arc therapy with robotic sterotactic radiation therapy in hepatocellular carcinoma", *Radiation Oncology Journal* 2015

[Sakata20] Yukinobu Sakata et al. "A machine learning-based real-time tumour tracking system for fluoroscopic gating of lung therapy", *Physics in Medicine & Biology*, 2020

[Keall] Paul J Keall et al. "The Management of Respiratory Motion in Radiation Oncology Report of AAPM Task Group 76", *Med. Phys*, 2006

[Mori] Shinichiro Mori et al. "Motion Management in Particle Therapy", *Med Phys*. 2018

[Lubeck] Illustration adapted from http://www.imi.uni-luebeck.de/en/content/simulation-and-evaluation-impact-breathing-motion-thoracic-dose-distributions-different-radi

Thank you for your attention!