ACPSEM CPD Endorsed Activity

Australasian College of Physical Scientists & Engineers in Medicine

MIRSIG

ASMIRT APPROVED CPD PROGRAM
Appellation Code: SGHCCC-001544-2020

The ACPSEM Medical Image Registration Special Interest Group (MIRSIG) Online Webinars

The **current seminar** 1200, Tue , Tue 6th October 2020, is chaired by Adam Yeo

- Talk 2: **"Dose accumulation: Quantifying the uncertainty and identifying its applications"**

Presented by Nick Lowther(Physics)

Webinar activities!!

-Use the "Q&A" to ask questions!

Live Poll!

Poll information will be used to confirm CPD, so it is important to participate!

Post webinar survey!

Please answer survey when email is sent

Seminar material available online!

Please see https://www.acpsem.org.au/About-the-College/Special-Interest-Groups/MIRSIG

Be more involved!

1. MIRSIG welcomes professions from all disciplines, including radiation therapists and radiation oncologists
2. Sign up to the MIRSIG mailing list (https://www.acpsem.org.au/Home , click myACPSEM, click speciality groups, tick MIRSIG)
3. Join MIRSIG as a member, email mirsig@acpsem.org.au

Dose accumulation: Quantifying the uncertainty and identifying its applications

MIRSIG October 2020 webinar

Nick Lowther, PhD

ROMP registrar, Capital & Coast District Health Board, Wellington, New Zealand

This webinar is based on my PhD research: *Optimization of the treatment quality in head-and-neck radiation oncology*

[1] Lowther, N.J., Marsh, S.H. and Louwe, R.J., 2020. Quantifying the dose accumulation uncertainty after deformable image registration in head-and-neck radiotherapy. *Radiotherapy and Oncology*, *143*, pp.117-125.

[2] Lowther, N.J., Marsh, S.H. and Louwe, R.J., 2020. Dose accumulation to assess the validity of treatment plans with reduced margins in radiotherapy of head and neck cancer. *Physics and Imaging in Radiation Oncology*, *14*, pp.53-60.

[3] Lowther, N.J., Hamilton, D.A., Kim, H., Evans, J.M., Marsh, S.H. and Louwe, R.J., 2019. Monitoring anatomical changes of individual patients using statistical process control during head-and-neck radiotherapy. *Physics and Imaging in Radiation Oncology*, *9*, pp.21-27.

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Dr Rob Louwe – *clinical supervisor*

Dr Steven Marsh – *academic supervisor*

CCDHB medical physics team

Prof Kristy Brock – *thesis examiner*

Prof Marianne Aznar – *thesis examiner*

Capital & Coast District Health Board
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UC UNIVERSITY OF CANTERBURY
Te Whare Wānanga o Waitaha
CHRISTCHURCH NEW ZEALAND

Disclaimers

- The author has no conflicts of interest to report
- This webinar builds upon the previous MIRSIG webinars and assumes familiarity with DIR and its role in deformable dose accumulation/DIR-facilitated dose accumulation
- This webinar aims to provide education on DIR-facilitated dose accumulation using our research as case studies

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Learning objectives:

- Identify different **methods** of DIR-facilitated dose accumulation
- Demonstrate awareness of a method that can be used to estimate the **uncertainty in DIR-facilitated dose accumulation**
- Understand **potential applications** of DIR-facilitated dose accumulation
- Demonstrate awareness of the **remaining risks and uncertainties** in DIR-facilitated dose accumulation

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Overview

1. Background
    - *Deformable dose accumulation/DIR-facilitated dose accumulation*
2. Quantifying the uncertainty in DIR-facilitated dose accumulation
3. Applications of DIR-facilitated dose accumulation
    - *Assessing the validity of reduced PTV margins*
    - *Towards efficient ART*
4. Remaining uncertainties

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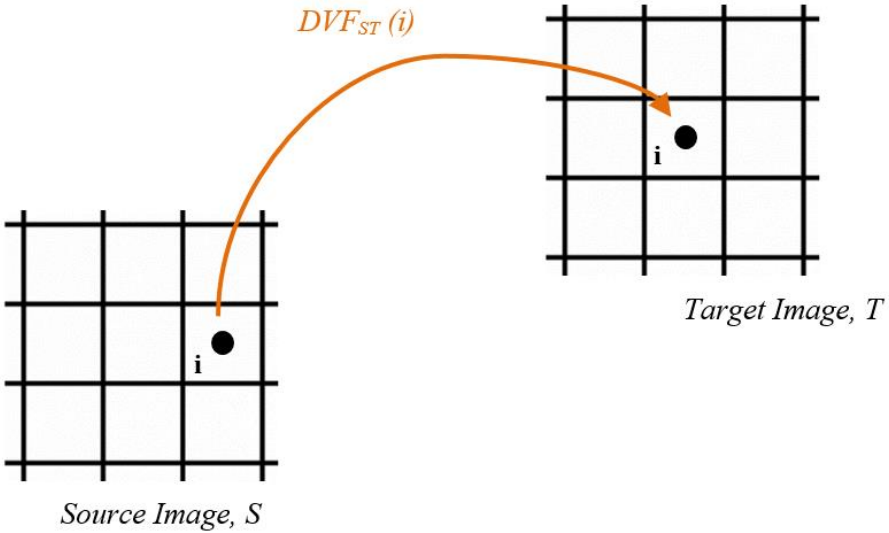
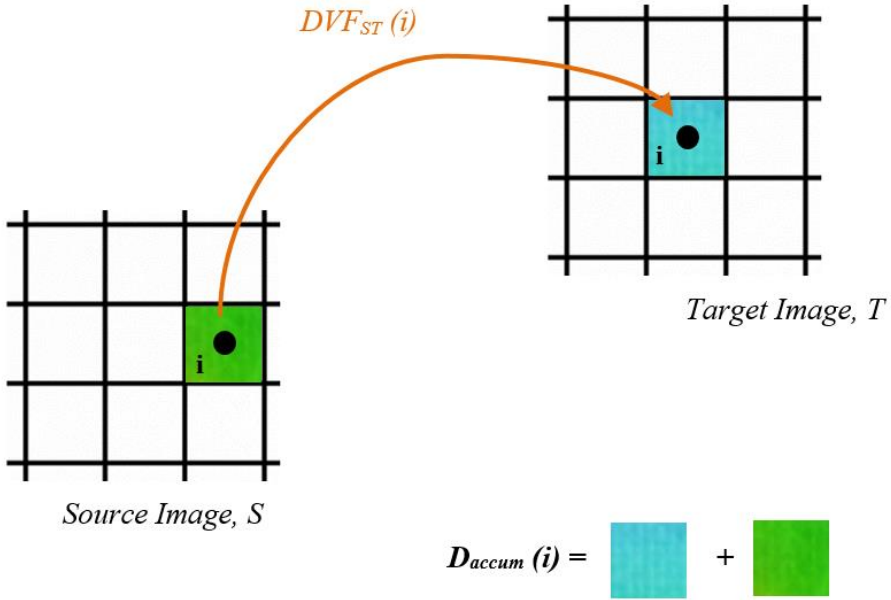
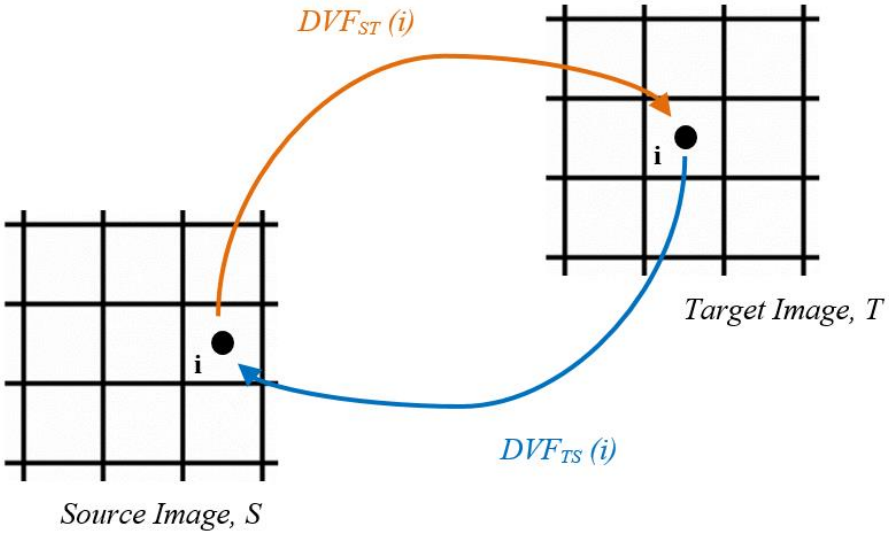
DIR-facilitated dose accumulation



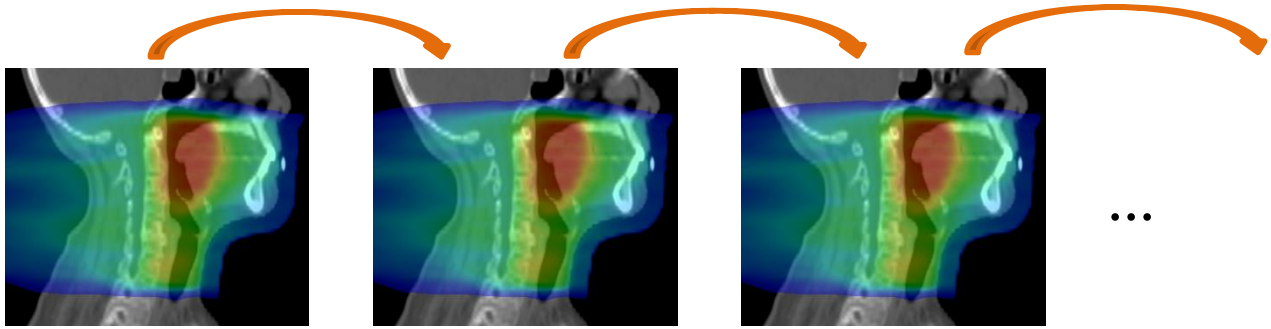
DIR-facilitated dose accumulation



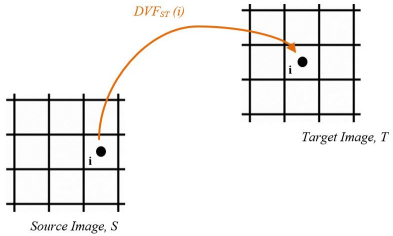
DIR-facilitated dose accumulation



Chronological DIR-facilitated dose accumulation

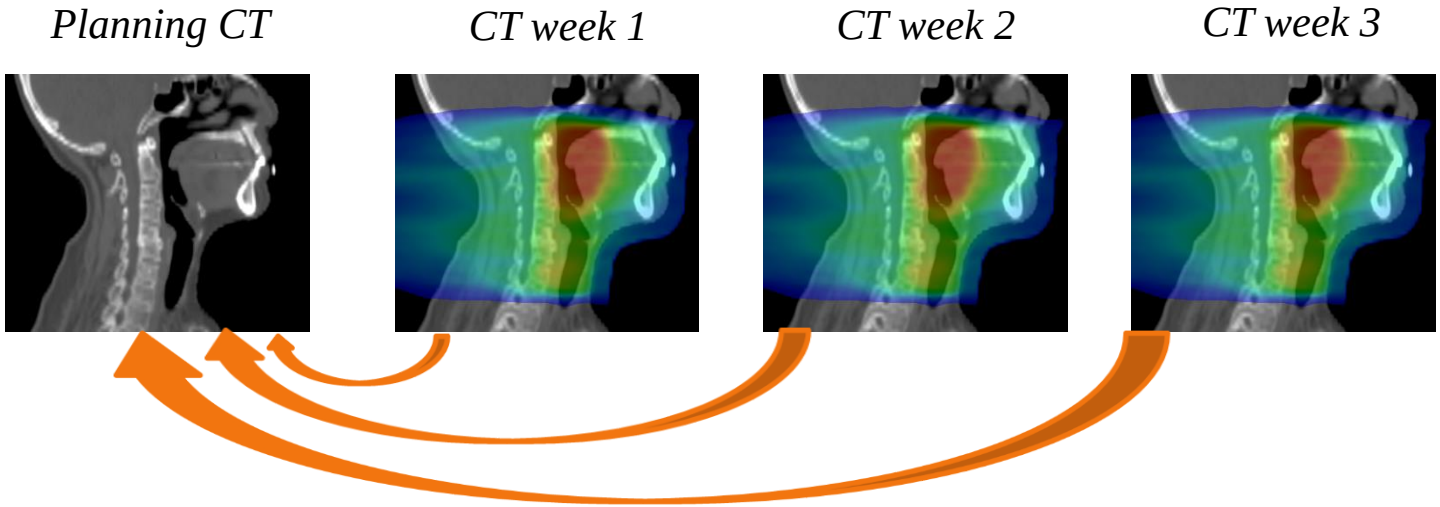


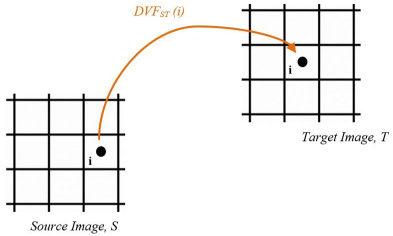
CT week 1 *CT week 2* *CT week 3*



1. Background

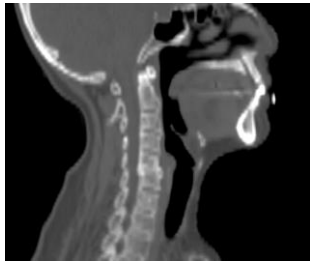
All-to-one DIR-facilitated dose accumulation

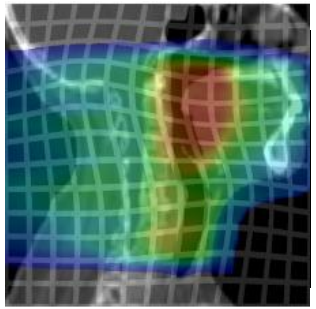


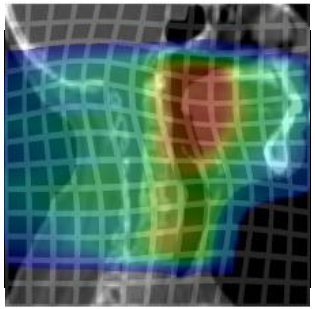


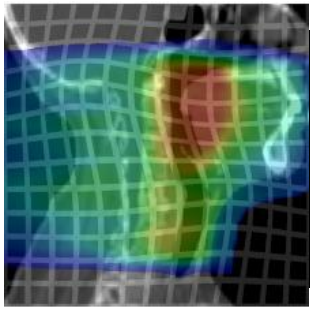
DIR-facilitated dose accumulation

Planning CT



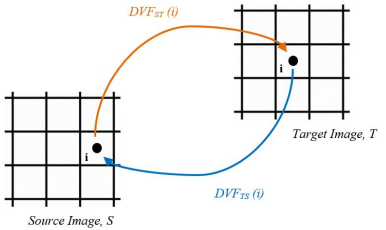






Not restricted to CTs, for example:

- CBCTs (with HU correction)
- Synthetic/deformed CTs



2. DIR-facilitated dose accumulation uncertainty

Radiotherapy and Oncology 143 (2020) 117–125

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Original Article

Quantifying the dose accumulation uncertainty after deformable image registration in head-and-neck radiotherapy

Nicholas J. Lowther [a,b], Steven H. Marsh [b], Robert J.W. Louwe [a,*]

[a] *Wellington Blood and Cancer Centre, Department of Radiation Oncology, Wellington; and* [b] *University of Canterbury, School of Physical and Chemical Sciences, Christchurch, New Zealand*

2. DIR-facilitated dose accumulation uncertainty

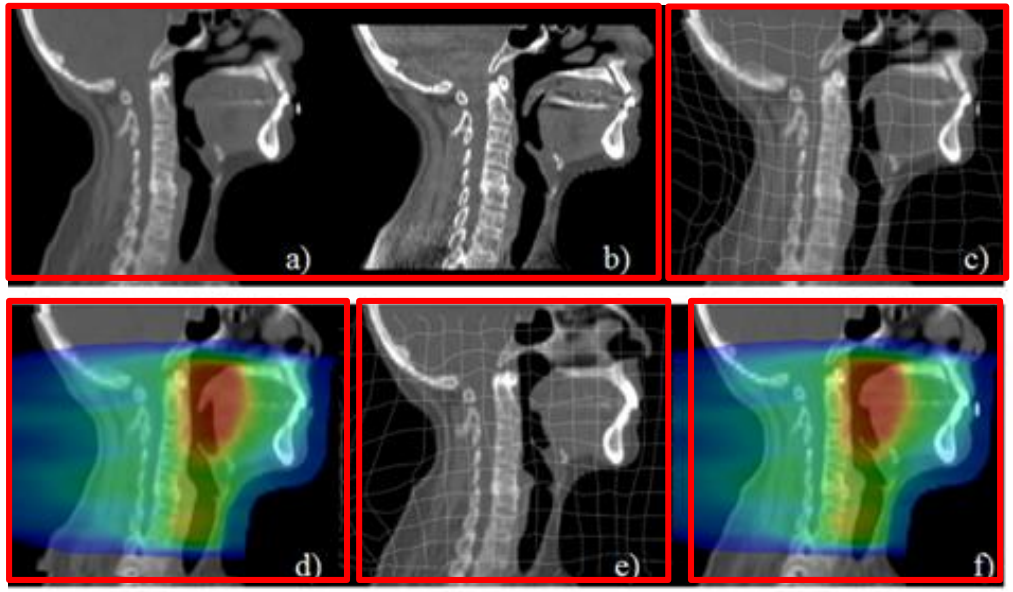
- Literature has shown that the *delivered dose* may deviate from the *planned dose* due to anatomical changes

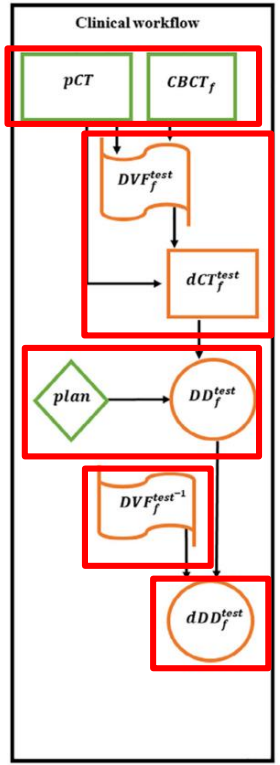
- DIR-facilitated dose accumulation can be applied to estimate the *delivered dose* and verify the validity of the treatment plan

- However, the accuracy of DIR-facilitated dose accumulation is seldom quantified and no literature existed on its accuracy specifically for the intended HNRT dose accumulation procedure at Wellington Hospital

2. DIR-facilitated dose accumulation uncertainty

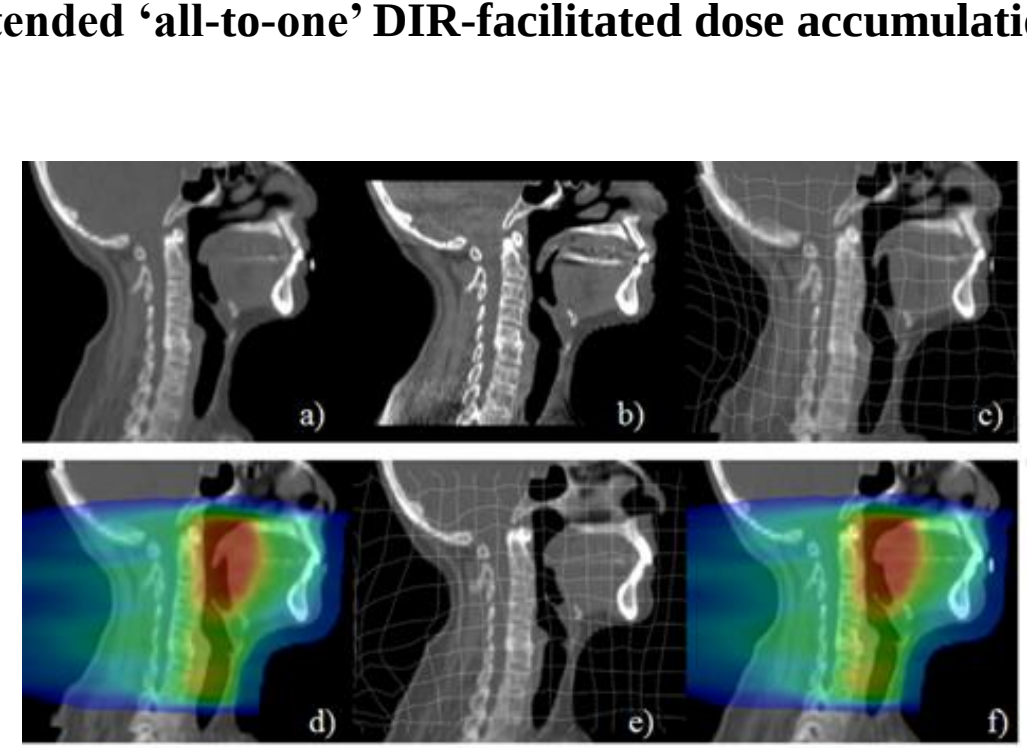
Intended ‘all-to-one’ DIR-facilitated dose accumulation workflow

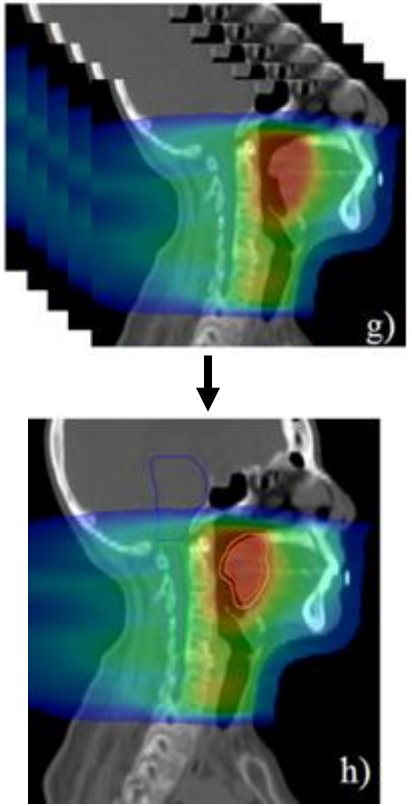




2. DIR-facilitated dose accumulation uncertainty

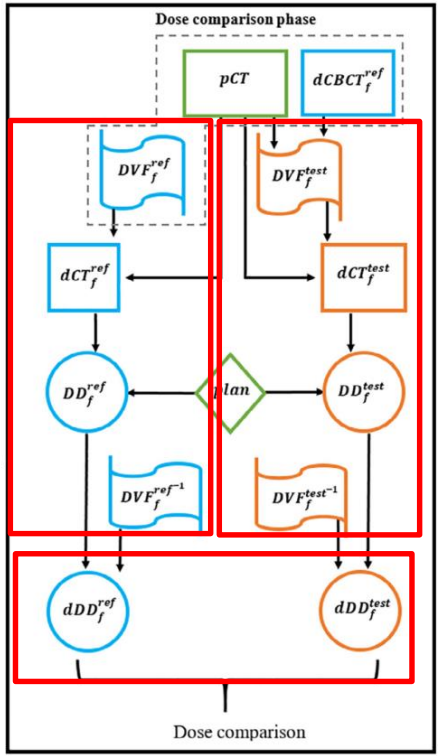
Intended ‘all-to-one’ DIR-facilitated dose accumulation workflow





2. DIR-facilitated dose accumulation uncertainty

Schematic of how the uncertainty in the DIR-facilitated dose accumulation was assessed:



We tested whether SmartAdapt DIR can reproduce a reference dose distribution

The initialization phase generated the same input data to ensure a fair dose comparison

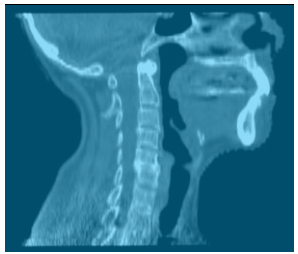
Reference DIR based on B-Spline

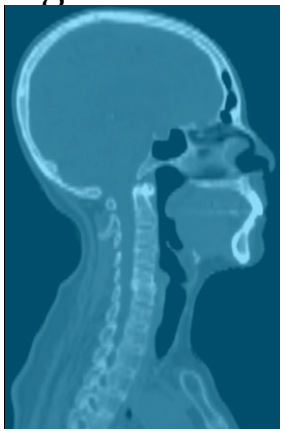
Varian SmartAdapt DIR based on Demons

2. DIR-facilitated dose accumulation uncertainty

Explanation of how the uncertainty in the DIR-facilitated dose accumulation was assessed:

1) Generate a reference CBCT and a reference deformed CT using *in silico* deformations based on clinically observed anatomical changes

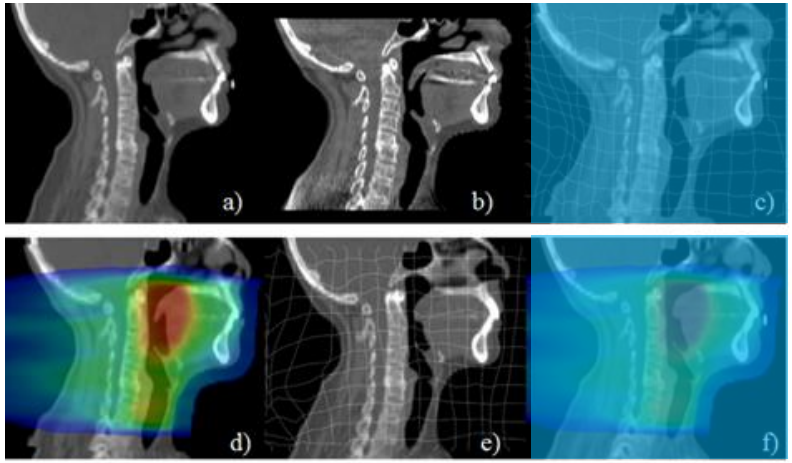




2. DIR-facilitated dose accumulation uncertainty

Explanation of how the uncertainty in the DIR-facilitated dose accumulation was assessed:

2) Using the reference deformed CT, generate a reference reconstructed dose



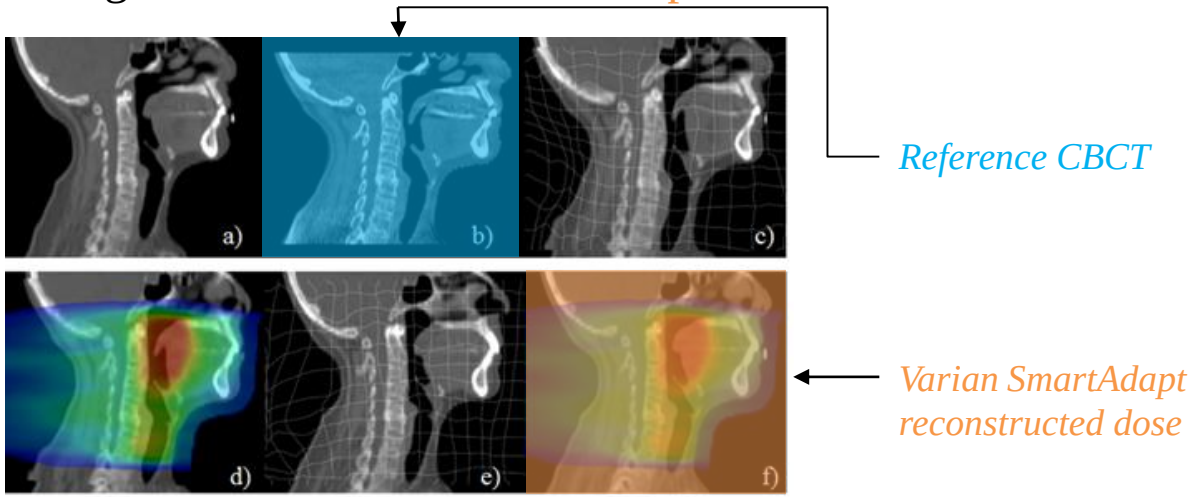
Reference deformed CT

Reference reconstructed dose

2. DIR-facilitated dose accumulation uncertainty

Explanation of how the uncertainty in the DIR-facilitated dose accumulation was assessed:

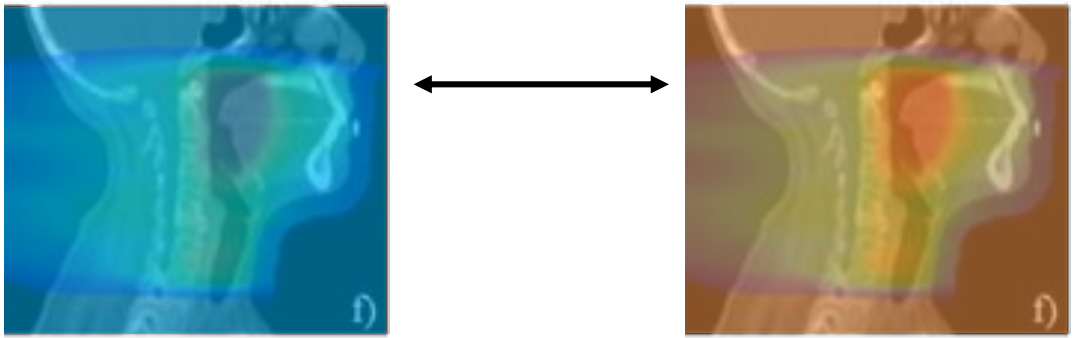
3) Using the reference CBCT, generate an Varian SmartAdapt reconstructed dose



2. DIR-facilitated dose accumulation uncertainty

Explanation of how the uncertainty in the DIR-facilitated dose accumulation was assessed:

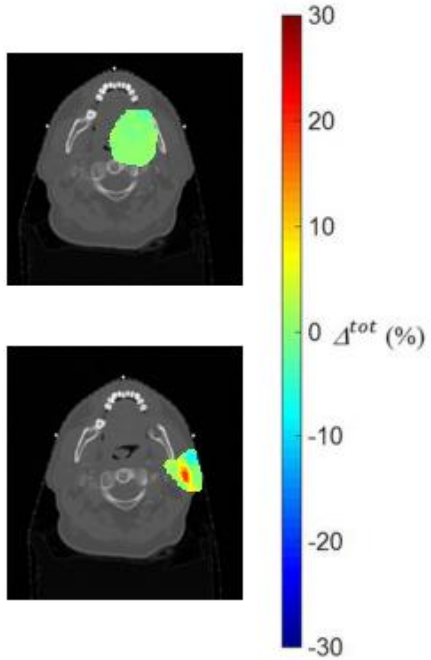
4) Compare the reference reconstructed dose against the Varian SmartAdapt reconstructed dose

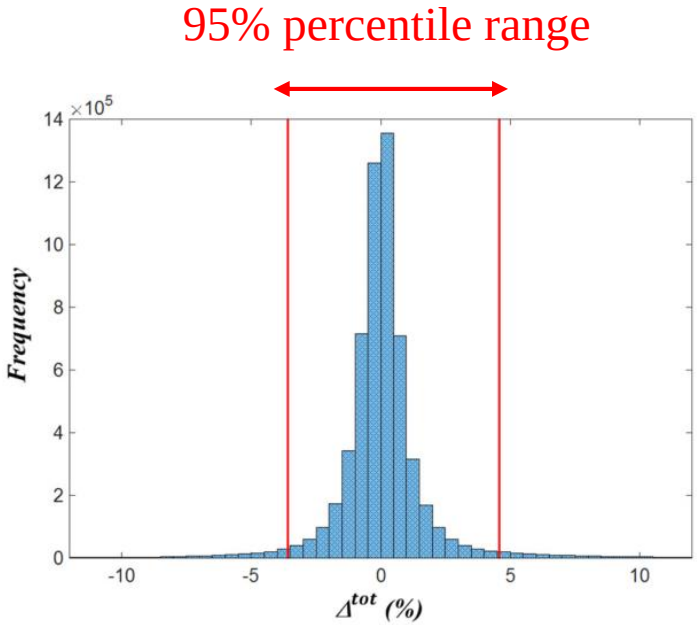


DIR based on B-Spline *DIR based on Demons*

2. DIR-facilitated dose accumulation uncertainty

Structure	n
High-dose PTV	11
Intermediate-dose PTV	4
Low-dose PTV	12
High-dose CTV	11
Intermediate-dose CTV	4
Low-dose CTV	12
Brainstem PRV	12
Spinal cord PRV	12
Brainstem	12
Spinal cord	12
Ipsilateral PG	14
Contralateral PG	10
Ipsilateral SMG	13
Contralateral SMG	10
All structures	149



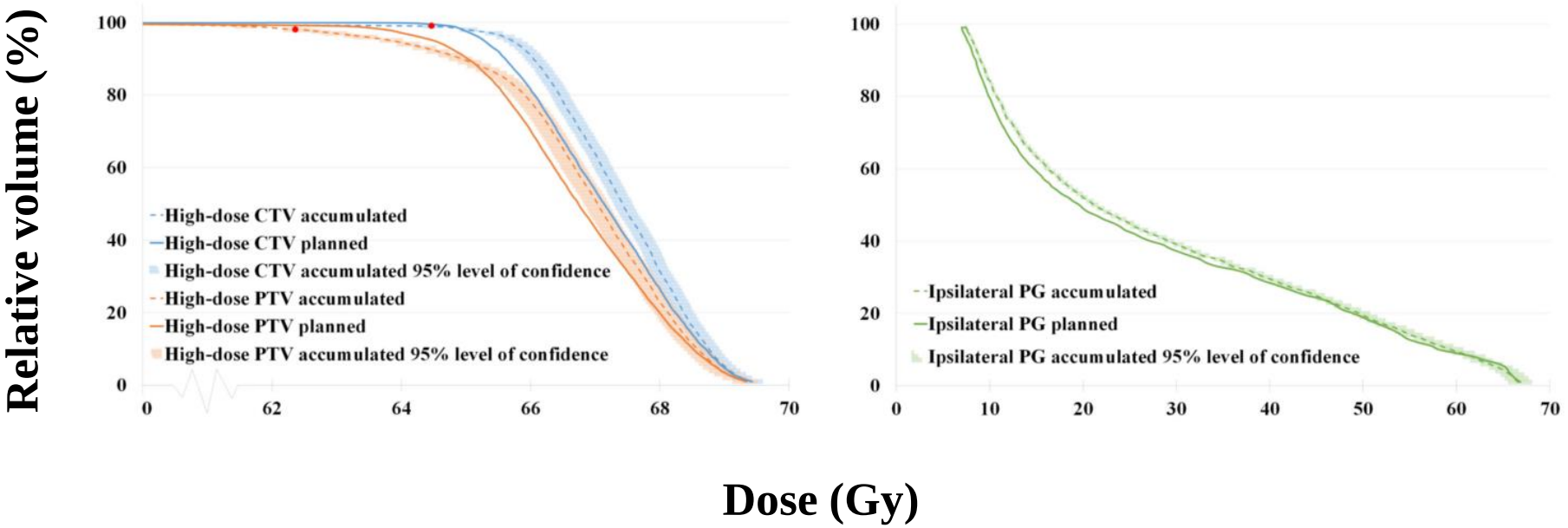


Δ^{tot} = *dose diff. rel. to planned dose*

2. DIR-facilitated dose accumulation uncertainty

		Single fraction reconstructed dose uncertainty Δ^{tot} (%), *inverse consistent voxels*		Uncertainty in the accumulated dose at the end of treatment uA^S (%), *inverse consistent voxels*	
Structure	**n**	**median**	**95% percentile range**	**median**	**95% percentile range**
High-dose PTV	11	0.0	-2.0; +1.6	0.0	-0.4; +0.3
Intermediate-dose PTV	4	-0.1	-2.9; +1.4	-0.1	-0.5; +0.3
Low-dose PTV	12	0.0	-3.1; +2.7	0.0	-0.6; +0.5
High-dose CTV	11	0.1	-1.3; +1.5	0.1	-0.2; +0.3
Intermediate-dose CTV	4	0.0	-1.7; +1.2	0.0	-0.3; +0.2
Low-dose CTV	12	0.0	-1.9; +2.0	0.0	-0.3; +0.4
Brainstem PRV	12	0.8	-13.7; +19.5	0.8	-2.5; +3.6
Spinal cord PRV	12	0.4	-6.7; +8.5	0.4	-1.2; +1.6
Brainstem	12	1.0	-15.6; +21.0	1.0	-2.8; +3.8
Spinal cord	12	0.4	-7.2; +9.0	0.4	-1.3; +1.6
Ipsilateral PG	14	0.6	-10.5; +14.4	0.6	-1.9; +2.6
Contralateral PG	10	0.5	-10.4; +12.7	0.5	-1.9; +2.3
Ipsilateral SMG	13	-0.1	-5.5; +3.3	-0.1	-1.0; +0.6
Contralateral SMG	10	-0.1	-3.6; +5.5	-0.1	-0.7; +1.0
All structures	149	0.0	-3.6; +4.6	0.0	-0.7; +0.8

2. DIR-facilitated dose accumulation uncertainty



2. DIR-facilitated dose accumulation uncertainty

- Quantified the accuracy of the DIR-facilitated *accumulated dose*

- We can use the estimated accuracy in a clinical implementation of dose accumulation

3. Applications of DIR-facilitated dose accumulation

Validity of a PTV margin reduction

Physics and Imaging in Radiation Oncology 14 (2020) 53–60

Contents lists available at ScienceDirect

Physics and Imaging in Radiation Oncology

journal homepage: www.elsevier.com/locate/phro

Dose accumulation to assess the validity of treatment plans with reduced margins in radiotherapy of head and neck cancer

Nicholas J. Lowther[a,b], Steven H. Marsh[b], Robert J.W. Louwe[a,*]

[a] Wellington Blood and Cancer Centre, Department of Radiation Oncology, Wellington, New Zealand
[b] University of Canterbury, School of Physical and Chemical Sciences, Christchurch, New Zealand

3. Applications of DIR-facilitated dose accumulation

Validity of a PTV margin reduction

Rationale for our study

- Literature reported reduced treatment toxicity in HNRT with 5 to 3 mm PTV margin reduction but the loco-regional control was not preserved in all studies

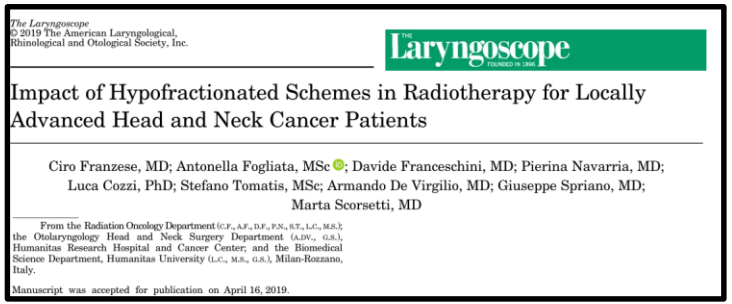
Original article

The impact of margin reduction on outcome and toxicity in head and neck cancer patients treated with image-guided volumetric modulated arc therapy (VMAT)

Arash Navran [a], Wilma Heemsbergen [a,b], Tomas Janssen [a], Olga Hamming-Vrieze [a], Marcel Jonker [a], Charlotte Zuur [c], Marcel Verheij [a], Peter Remeijer [a], Jan-Jakob Sonke [a], Michiel van den Brekel [c], Abrahim Al-Mamgani [a,*]

[a] Department of Radiation Oncology, Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Amsterdam; [b] Department of Radiation Oncology, Erasmus MC Cancer Institute, Rotterdam; and [c] Department of Head and Neck Surgery, Netherlands Cancer Institute, Amsterdam, The Netherlands

Accepted 22 June 2018



The Laryngoscope

Impact of Hypofractionated Schemes in Radiotherapy for Locally Advanced Head and Neck Cancer Patients

Ciro Franzese, MD; Antonella Fogliata, MSc; Davide Franceschini, MD; Pierina Navarria, MD; Luca Cozzi, PhD; Stefano Tomatis, MSc; Armando De Virgilio, MD; Giuseppe Spriano, MD; Marta Scorsetti, MD

From the Radiation Oncology Department (C.F., A.F., D.F., P.N., S.T., L.C., M.S.); the Otolaryngology Head and Neck Surgery Department (A.DV., G.S.), Humanitas Research Hospital and Cancer Center; and the Biomedical Science Department, Humanitas University (L.C., M.S., G.S.), Milan-Rozzano, Italy.

Manuscript was accepted for publication on April 16, 2019.

ORIGINAL ARTICLE

HEAD & NECK JOURNAL OF THE SCIENCES AND SPECIALTIES OF THE HEAD AND NECK

Long-term experience with reduced planning target volume margins and intensity-modulated radiotherapy with daily image-guidance for head and neck cancer

Allen M. Chen, MD,[1*] Yao Yu, MD,[1] Megan E. Daly, MD,[1] D. Gregory Farwell, MD,[2] Stanley H. Benedict, PhD,[1] James A. Purdy, PhD[1]

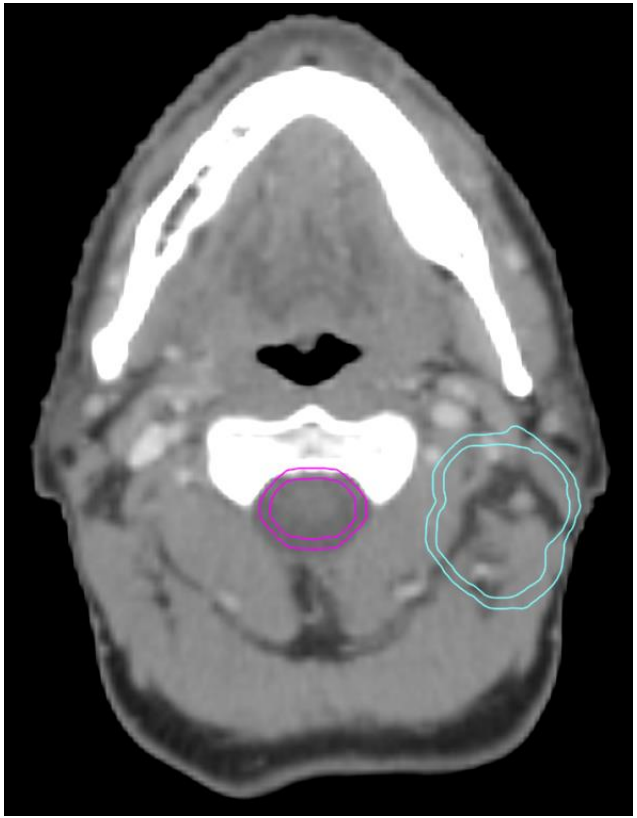
[1]Department of Radiation Oncology, University of California Davis Comprehensive Cancer Center, Sacramento, California, [2]Department of Otolaryngology – Head and Neck Surgery, University of California Davis Comprehensive Cancer Center, Sacramento, California.

Accepted 22 October 2013

3. Applications of DIR-facilitated dose accumulation

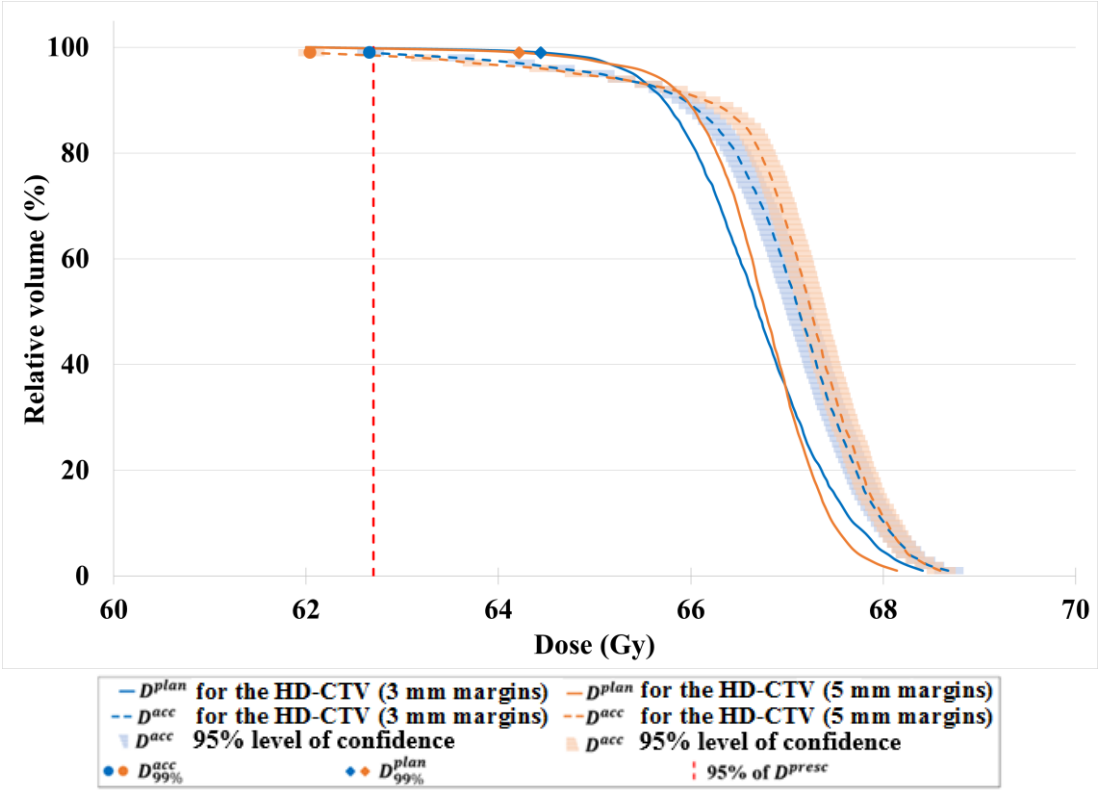
Validity of a PTV margin reduction

- VMAT plans for 12 patients: 3 and 5 mm PTV and planning risk volume (PRV) margin plans
- The DIR-facilitated dose accumulation method described above was used to accumulate dose
- CTV coverage was assessed using the DVH metric $D_{99\%}$, consistent with literature [vanKranen2016]
- 1% of the CTV could represent a large absolute volume, so coverage was also assessed by individual voxels



3. Applications of DIR-facilitated dose accumulation

Validity of a PTV margin reduction



3. Applications of DIR-facilitated dose accumulation

Validity of a PTV margin reduction

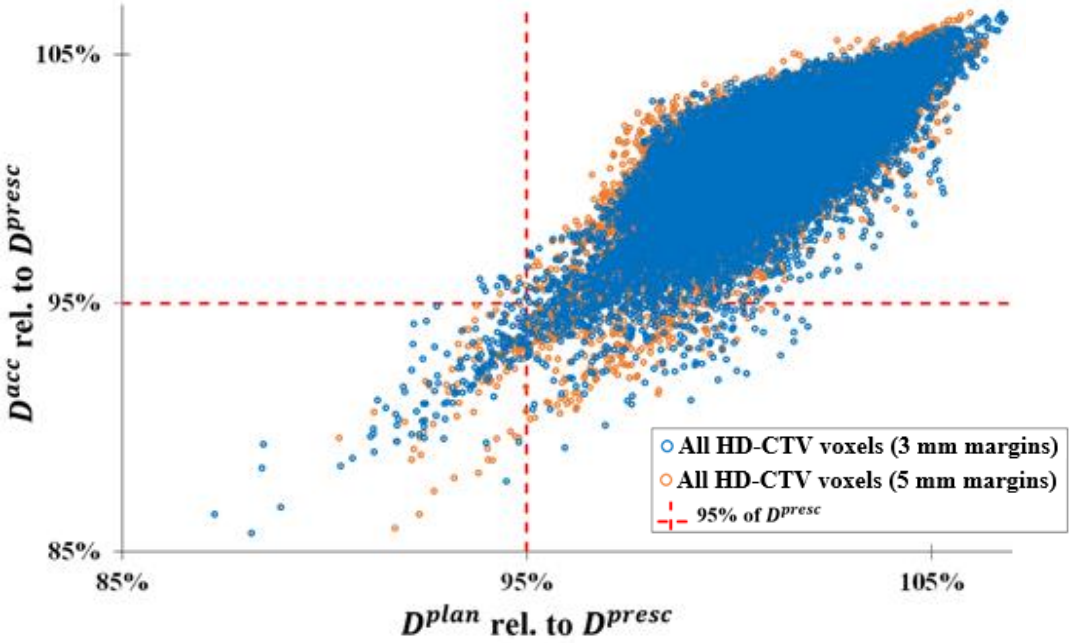
- The number of cases where the accumulated dose $D_{99\%}$ of a **CTV** was less than 95% D^{presc} was:
  - Statistically significant for one 5 mm margin plan
  - Borderline statistically significant for two 3 mm margin plans

Statistically significant = the accumulated dose 95% level of confidence does not contain 95% D^{presc}

3. Applications of DIR-facilitated dose accumulation

Validity of a PTV margin reduction

However for many cases, the accumulated dose included a substantial number of CTV voxels receiving less than 95% of the prescribed dose



3. Applications of DIR-facilitated dose accumulation

Validity of a PTV margin reduction

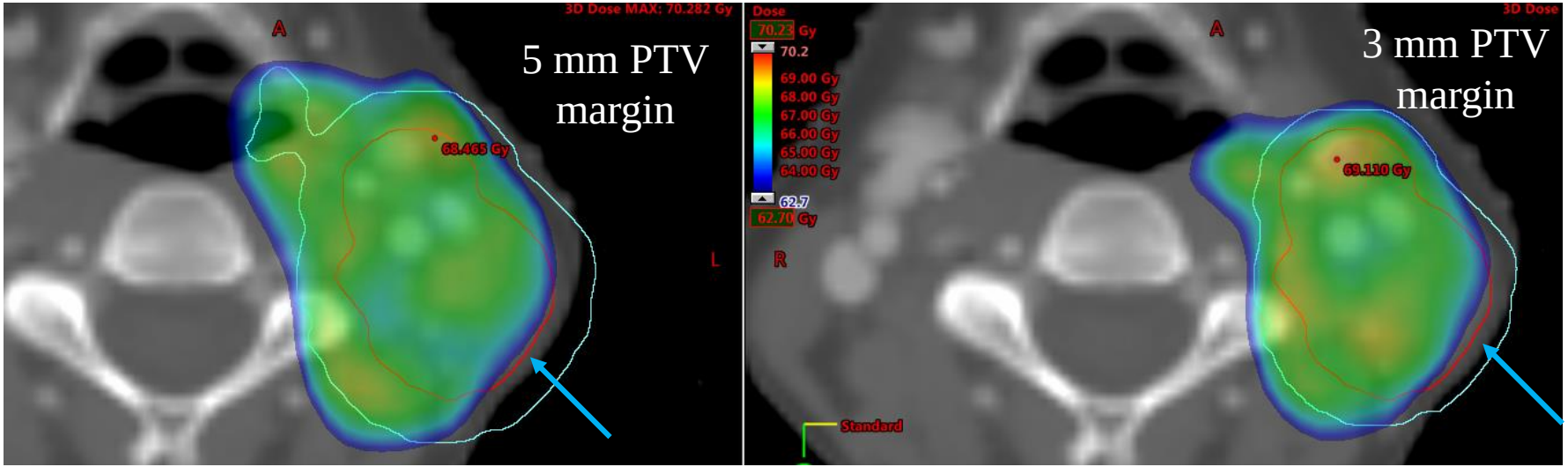
Loss in target coverage during treatment was:

- Very patient specific due to the interplay between local fluence, dose delivered per gantry angle, contribution of scatter and anatomical changes
- Independent of margin expansion and tightness of target volume coverage at planning increased the risk of clinically unacceptable dose delivery
- Predominantly occurring in the sub-dermal region

3. Applications of DIR-facilitated dose accumulation

Validity of a PTV margin reduction

For many cases, the accumulated dose included a substantial number of CTV voxels receiving less than 95% of the prescribed dose



3. Applications of DIR-facilitated dose accumulation

Validity of a PTV margin reduction

Sub-dermal/dermal recurrences in literature

ORIGINAL ARTICLE

HEAD & NECK

JOURNAL OF THE SCIENCES AND SPECIALTIES OF THE HEAD AND NECK

Long-term experience with reduced planning target volume margins and intensity-modulated radiotherapy with daily image-guidance for head and neck cancer

Allen M. Chen, MD,[1*] Yao Yu, MD,[1] Megan E. Daly, MD,[1] D. Gregory Farwell, MD,[2] Stanley H. Benedict, PhD,[1] James A. Purdy, PhD[1]

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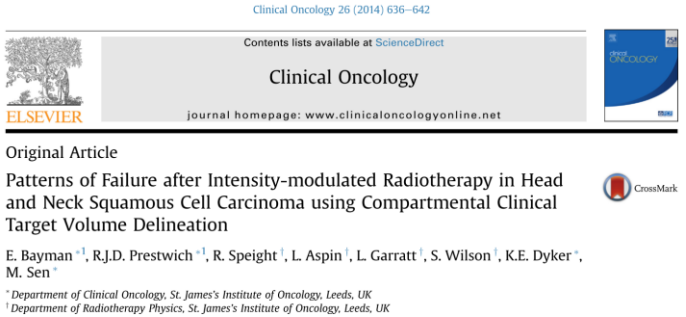
***9** marginal LR recurrences: **4** dermal*



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ELSEVIER

Original Article

Patterns of Failure after Intensity-modulated Radiotherapy in Head and Neck Squamous Cell Carcinoma using Compartmental Clinical Target Volume Delineation

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***1** marginal LR recurrence: **1** dermal*

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Original Article

OXFORD

Original Article

Patterns of failure after postoperative intensity-modulated radiotherapy for locally advanced and recurrent head and neck cancer

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***5** marginal LR recurrences: **3** dermal*

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Radiotherapy and Oncology

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ELSEVIER

Phase II trial

Dose–volume analysis of locoregional recurrences in head and neck IMRT, as determined by deformable registration: A prospective multi-institutional trial

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***9** marginal LR recurrences: **2** dermal*

3. Applications of DIR-facilitated dose accumulation

Validity of a PTV margin reduction

- We did not observe a systematic difference in plan robustness for anatomical changes between 5 and 3 mm PTV/PRV margins

- A safe PTV margin reduction from 5 to 3 mm in HNRT may be achieved but requires **individual patient dose monitoring** considering the loss in coverage was patient specific

Using DIR-facilitated dose accumulation

3. Applications of DIR-facilitated dose accumulation

Towards efficient ART

ELSEVIER

Seminars in RADIATION ONCOLOGY

Deformable Registration for Dose Accumulation

Indrin J. Chetty, PhD,* and Mihaela Rosu-Bubulac, PhD†

As deformable image registration makes its way into the clinical routine, the summation of doses from fractionated treatment regimens to evaluate cumulative doses to targets and healthy tissues is also becoming a frequently utilized tool in the context of image-guided adaptive radiotherapy. Accounting for daily geometric changes using deformable image registration and dose accumulation potentially enables a better understanding of dose-volume-effect relationships, with the goal of translation of this knowledge to personalization of treatment, to further enhance treatment outcomes. Treatment adaptation involving image deformation requires patient-specific quality assurance of the image registration and dose accumulation processes, to ensure that uncertainties in the 3D dose distributions are identified and appreciated from a clinical relevance perspective. While much research has been devoted to identifying and managing the uncertainties associated with deformable image registration and dose accumulation approaches, there are still many unanswered questions. Here, we provide a review of current deformable image registration and dose accumulation techniques, and related clinical application. We also discuss salient issues that need to be deliberated when applying deformable algorithms for dose mapping and accumulation in the context of adaptive radiotherapy and response assessment.

Semin Radiat Oncol 29:198–208

ELSEVIER

Seminars in RADIATION ONCOLOGY

Adaptive Radiotherapy for Anatomical Changes

Jan-Jakob Sonke, PhD,* Marianne Aznar, PhD,†,‡ and Coen Rasch, MD, PhD§

The anatomy of cancer patients changes between radiation treatment planning and delivery as well as over the course of radiotherapy. Adaptive radiotherapy (ART) aims to deliver radiation accurately and precisely in the presence of such changes. To that end, ART uses an imaging feedback loop to quantify these changes and modify the treatment plan accordingly. This paper provides an overview of anatomical changes occurring over the course of therapy and various adaptive strategies developed to account for those. Moreover, residual uncertainties present in adaptive radiotherapy are discussed as well as required tools, potential pitfalls and remaining challenges.

Semin Radiat Oncol 29:245–257

Radiotherapy and Oncology 143 (2020) 117–125

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ELSEVIER

Original Article

Quantifying the dose accumulation uncertainty after deformable image registration in head-and-neck radiotherapy

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[a] Wellington Blood and Cancer Centre, Department of Radiation Oncology, Wellington; and [b] University of Canterbury, School of Physical and Chemical Sciences, Christchurch, New Zealand

Toward adaptive radiotherapy for head and neck patients: Uncertainties in dose warping due to the choice of deformable registration algorithm

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www.redjournal.org

Physics and Imaging in Radiation Oncology 14 (2020) 53–60

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Physics and Imaging in Radiation Oncology

journal homepage: www.elsevier.com/locate/phro

ELSEVIER

phiRO

Dose accumulation to assess the validity of treatment plans with reduced margins in radiotherapy of head and neck cancer

Nicholas J. Lowther[a,b], Steven H. Marsh[b], Robert J.W. Louwe[a,*]

[a] *Wellington Blood and Cancer Centre, Department of Radiation Oncology, Wellington, New Zealand*

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760 Med. Phys. 42 (2), February 2015 0094-2405/2015/42(2)/760/10 760

Int. J. Radiation Oncology Biol. Phys., Vol. 76, No. 3, Supplement, pp. S135–S139, 2010

0360-3016/10/$–see front matter

doi:10.1016/j.ijrobp.2009.06.093

QUANTEC: VISION PAPER

ACCURATE ACCUMULATION OF DOSE FOR IMPROVED UNDERSTANDING OF RADIATION EFFECTS IN NORMAL TISSUE

DAVID A. JAFFRAY, PH.D.,* PATRICIA E. LINDSAY, PH.D.,* KRISTY K. BROCK, PH.D.,* JOSEPH O. DEASY, PH.D.,† AND W. A. TOMÉ, PH.D.‡

From the *Radiation Medicine Program, Princess Margaret Hospital, Department of Radiation Oncology, University of Toronto, Toronto, Ontario, Canada; †Department of Radiation Oncology, Washington University, St. Louis, MO; and ‡Departments of Human Oncology and Medical Physics, University of Wisconsin School of Medicine and Public Health, Madison, WI

Physics Contribution

Head and Neck Margin Reduction With Adaptive Radiation Therapy: Robustness of Treatment Plans Against Anatomy Changes

Simon van Kranen, MSc,* Olga Hamming-Vrieze, MD,* Annelisa Wolf, PhD,* Eugène Damen, PhD,* Marcel van Herk, PhD,† and Jan-Jakob Sonke, PhD*

3. Applications of DIR-facilitated dose accumulation

Towards efficient ART

Different ART approaches

- **Offline**
  - *Triggered*

    Adapting the treatment when a "threshold" has been exceeded. E.g., non-rigid anatomical changes such as weight loss. Implementations of triggered offline adaption can include rescan/replans and average anatomy models.

  - *Scheduled*

    Adapting the treatment at a scheduled time-point(s). Implementations of scheduled offline adaption can also include rescan/replans and average anatomy models.

- **Online**
  - *Library of plans*

    Selecting the most appropriate plan from a collection of plans to account for the observed anatomical changes.

  - *Online replanning*

    Optimisation of the plan at every treatment fraction.

3. Applications of DIR-facilitated dose accumulation

Towards efficient ART

A common disadvantage of the current ART approaches

"...is the reliability of the criteria to identify patients for adaptation" *[Sonke2019]*

False negatives: Patients who would benefit from ART can go undetected

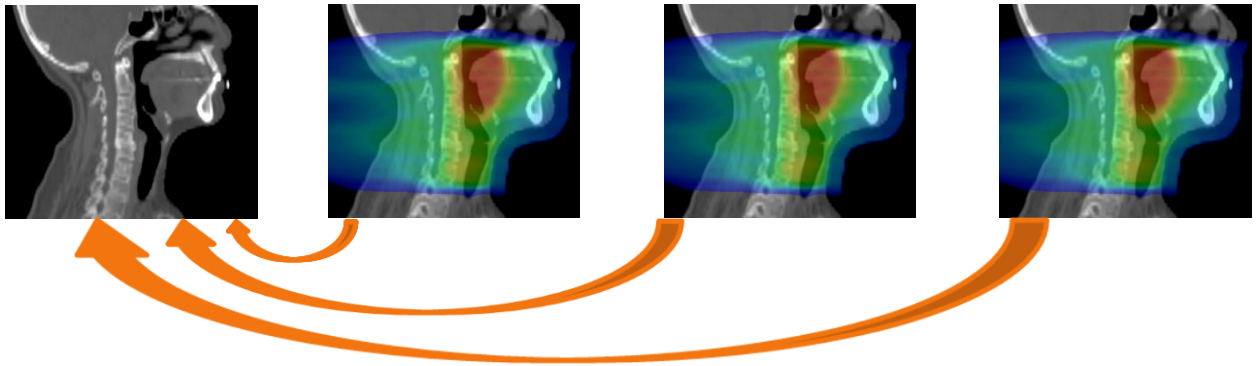
False positives: Unnecessary ART may result in a high-resource burden

3. Applications of DIR-facilitated dose accumulation

Towards efficient ART

Deformable dose accumulation

Reliable deformable dose accumulation that includes an estimate of its uncertainty may provide more efficient ART by processing patients' longitudinal changes



4. Remaining uncertainties

Uncertainties in DIR-facilitated dose accumulation

- **The underlying DVF** (*has been mentioned extensively during the MIRSIG webinars*)
  - Qualitative analyses can include checkerboard, overlap and image difference
  - Quantitative analyses can include target registration error (TRE), overlap metrics, Jacobian, etc.

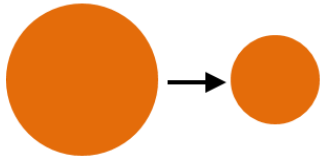
- **The underlying DVF (and DVF^{-1}) specifically for deformable dose accumulation**
  - Quantitative analyses can include the use of physical or *in-silico* phantoms as ground truth with subsequent dose comparison [Yeo2012] [Lowther2020] [Veiga2015]

4. Remaining uncertainties

Uncertainties in DIR-facilitated dose accumulation

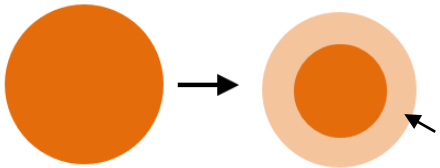
- **The modes of tumour regression**
  - *Elastic*

    The process whereby all tissue (tumour and normal) retreats concentrically with the tumour border including any subclinical microscopic malignant disease



  - *Inelastic*

    The process where the tumour boundary retreats concentrically but independently of the surrounding normal tissue, potentially leaving pockets of subclinical microscopic malignant disease

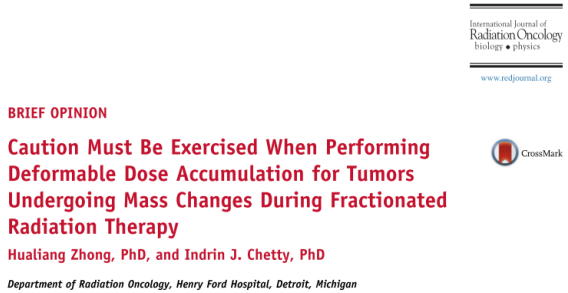


4. Remaining uncertainties

Uncertainties in DIR-facilitated dose accumulation

The majority of DIR algorithms, which are based on intensity similarity of the two image sets, will tend to align the border of the regressed tumour mass (or normal tissue) with that of the initial tumour and will:

- *For elastic regression*, impose the dose received by the regressed tumour to all voxels of the initial tumour which would create energy, and violate the principle that energy should be conserved



- *For inelastic regression*, in addition to the energy conservation limitation, will not appropriately account for dose to the tissues surrounding the regressed tumour mass

References

[Chen2014] Chen, A.M., Yu, Y., Daly, M.E., Farwell, D.G., H. Benedict, S. and Purdy, J.A., 2014. Long-term experience with reduced planning target volume margins and intensity-modulated radiotherapy with daily image-guidance for head and neck cancer. *Head & neck*, *36*(12), pp.1766-1772.

[Navran2018] Navran, A., Heemsbergen, W., Janssen, T., Hamming-Vrieze, O., Jonker, M., Zuur, C., Verheij, M., Remeijer, P., Sonke, J.J., van den Brekel, M. and Al-Mamgani, A., 2019. The impact of margin reduction on outcome and toxicity in head and neck cancer patients treated with image-guided volumetric modulated arc therapy (VMAT). *Radiotherapy and oncology*, 130, pp.25-31.

[Franzese2019] Franzese, C., Fogliata, A., Franceschini, D., Navarria, P., Cozzi, L., Tomatis, S., De Virgilio, A., Spriano, G. and Scorsetti, M., 2019. Impact of hypofractionated schemes in radiotherapy for locally advanced head and neck cancer patients. *The Laryngoscope*.

[vanKranen2016] van Kranen, S., Hamming-Vrieze, O., Wolf, A., Damen, E., van Herk, M. and Sonke, J.J., 2016. Head and neck margin reduction with adaptive radiation therapy: robustness of treatment plans against anatomy changes. *International Journal of Radiation Oncology* Biology* Physics*, *96*(3), pp.653-660.

[Chetty2019] Chetty, I.J. and Rosu-Bubulac, M., 2019, July. Deformable registration for dose accumulation. *In Seminars in radiation oncology* (Vol. 29, No. 3, pp. 198-208). WB Saunders.

[Sonke2019] Sonke, J.J., Aznar, M. and Rasch, C., 2019, July. Adaptive radiotherapy for anatomical changes. *In Seminars in radiation oncology* (Vol. 29, No. 3, pp. 245-257). WB Saunders.

[Zhong2017] Zhong, H. and Chetty, I.J., 2017. Caution must be exercised when performing deformable dose accumulation for tumors undergoing mass changes during fractionated radiation therapy. *International Journal of Radiation Oncology• Biology• Physics, 97*(1), pp.182-183.

[Jaffray2010] Jaffray, D.A., Lindsay, P.E., Brock, K.K., Deasy, J.O. and Tomé, W.A., 2010. Accurate accumulation of dose for improved understanding of radiation effects in normal tissue. *International Journal of Radiation Oncology* Biology* Physics*, *76*(3), pp.S135-S139.

[Veiga2015] Veiga, C., Lourenço, A.M., Mouinuddin, S., van Herk, M., Modat, M., Ourselin, S., Royle, G. and McClelland, J.R., 2015. Toward adaptive radiotherapy for head and neck patients: uncertainties in dose warping due to the choice of deformable registration algorithm. *Medical physics*, *42*(2), pp.760-769.

[vanKranen2016] van Kranen, S., Hamming-Vrieze, O., Wolf, A., Damen, E., van Herk, M. and Sonke, J.J., 2016. Head and neck margin reduction with adaptive radiation therapy: robustness of treatment plans against anatomy changes. *International Journal of Radiation Oncology* Biology* Physics*, *96*(3), pp.653-660.

The ACPSEM Medical Image Registration Special Interest Group (MIRSIG) Online Webinars

Questions and Answers from the October 2020 Webinar Chaired by Adam Yeo (Talk 2 by Nick Lowther)

Question 1: Which approach Is better to accumulate the dose on planning CT or sum the dose from the individual fraction?

Answers: Neither approach is necessarily better. It is important to consider what tools you have at your department. For example, we did not have access to HU corrected CBCTs so we opted to use the all-to-one planning CT approach. Regardless of accumulation method, it is important to assess and be aware of the dose accumulation uncertainties.

Of note, if you were to chronologically accumulate dose using previous 'synthetic/deformed' CTs, you may be introducing a systematic error. That error would be propagated through the accumulation chain. It is therefore preferable to use new DVFs for each registration in a chronological approach.

Question 2: How much of DVH accuracy by ART would translate into Clinical outcomes. What's tolerance to apply ART or noART?

Answers: This is likely to be a chicken and egg scenario. At this time, there is limited information on the *actually delivered dose* corresponding to clinical outcomes. It is hoped that reliable DIR-facilitated dose accumulation that includes an estimate of its uncertainty could provide more efficient ART (and therefore the tolerances to apply or not apply ART) by processing patients' longitudinal changes