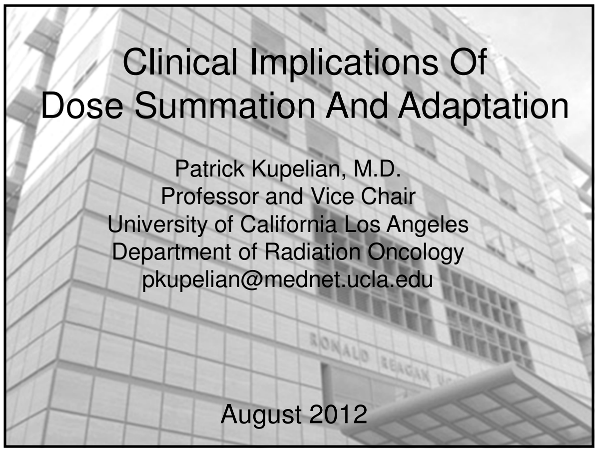


# Clinical Implications Of Dose Summation And Adaptation

Patrick Kupelian, M.D.
Professor and Vice Chair
University of California Los Angeles
Department of Radiation Oncology
pkupelian@mednet.ucla.edu

August 2012

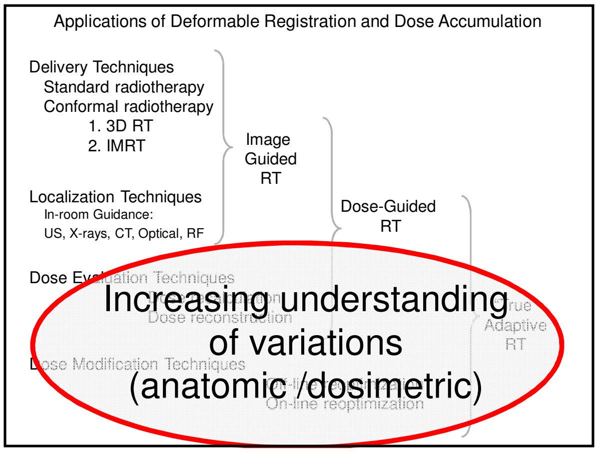
## Objectives

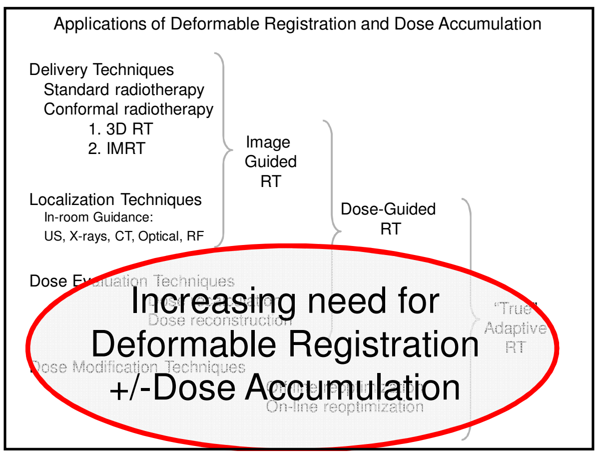
1. Understand the need for anatomy-based adaptation and methods to safely implement this in the clinic
2. Recognize the need for physiological-based adaptation and methods to safely implement this into the clinic
3. Appreciate the radiobiological limitations and concerns associated with dose summation, and adaptation
4. Describe the clinical implications of dose summation and adaptation on individual patient treatments, clinical trials, and outcomes assessment.

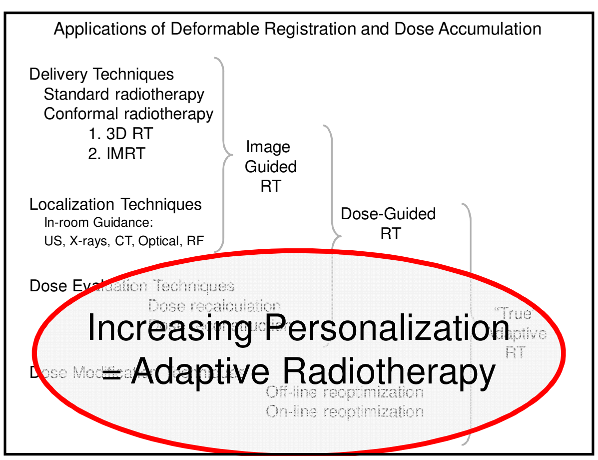
## Important Disclosures

Research grants / Honoraria / Advisory Board:

Accuray
Bayer Healthcare
Elekta
Varian Medical
Viewray Inc.


Applications of Deformable Registration and Dose Accumulation
Delivery Techniques
Standard radiotherapy
Conformal radiotherapy
1. 3D RT
2. IMRT
Localization Techniques
In-room Guidance:
US, X-rays, CT, Optical, RF
Image Guided RT
Dose-Guided RT
Dose Evaluation Techniques
Dose reconstruction
Dose Modification Techniques
On-line reoptimization
Adaptive RT
Increasing understanding of variations (anatomic /dosimetric)


Applications of Deformable Registration and Dose Accumulation
Delivery Techniques
Standard radiotherapy
Conformal radiotherapy
1. 3D RT
2. IMRT
Localization Techniques
In-room Guidance:
US, X-rays, CT, Optical, RF
Image Guided RT
Dose-Guided RT
Dose Evaluation Techniques
Dose reconstruction
Dose Modification Techniques
On-line reoptimization
"True" Adaptive RT
Increasing need for Deformable Registration +/-Dose Accumulation


Applications of Deformable Registration and Dose Accumulation
Delivery Techniques
Standard radiotherapy
Conformal radiotherapy
1. 3D RT
2. IMRT
Localization Techniques
In-room Guidance:
US, X-rays, CT, Optical, RF
Image Guided RT
Dose-Guided RT
Dose Evaluation Techniques
Dose recalculation
Off-line reoptimization
On-line reoptimization
"True" Adaptive RT
Increasing Personalization = Adaptive Radiotherapy

Applications of Deformable Registration and Dose Accumulation

DOCUMENTATION OF
“TRUE” DELIVERED DOSES

IMPLICATIONS FOR OUTCOMES ASSESSMENTS

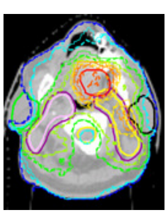
A TYPICAL RADIATION THERAPY COURSE

PRE-TREATMENT EVALUATION


“We’ve found a mass. The good news is we have weapons of mass destruction.”

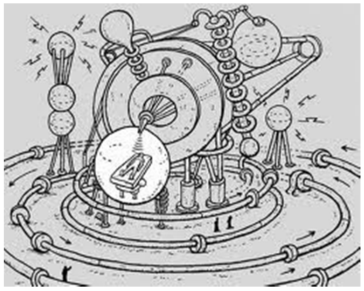
DESIGN TREATMENT DELIVERY PLAN

TREATMENT PLAN

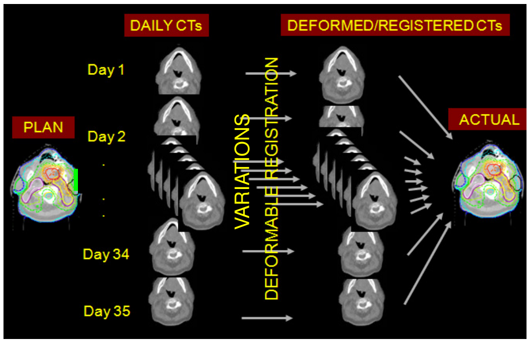


- Planned Doses
- Single snapshot
- Static Dose/Volume Information

RADIATION THERAPY DELIVERY-
TREATMENT COURSE



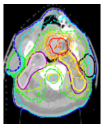
TREATMENT COURSE:
MULTIPLE REPEATS OF PLANNED DELIVERY



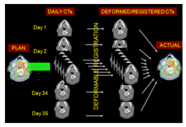

POST-TREATMENT EVALUATION

OUTCOMES EVALUATION
Cure / Toxicity

## OUTCOMES EVALUATION



PLANNED DOSE?



TRUE DOSE?

OUTCOMES:
Cure/Toxicity

Toxicity=
Quantec

## CLINICAL IMPLICATIONS: TOXICITY EVALUATIONS QUANTEC

(Quantitative Analysis of Normal Tissue Effects in the Clinic)


IJROBP, Vol. 76, No. 3, Supplement

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

0360-3016/10/$–see front matter

ELSEVIER

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

PLANNED DOSE VS TRUE DOSE ($D_A$)

PLAN VS TRUE DOSE - IMPLICATIONS:

**Current Practice:**

Study robustness of current RT deliveries
Better reporting of dose/volume data
Understand true dose correlations vs outcomes

↓

**Future Practice:**

Design of clinical trials: Dose prescriptions
Reporting of clinical trial results
Implementation of “true” Adaptive RT

Cancer/Radiothérapie 15 (2011) 555–559

Disponible en ligne sur ScienceDirect www.sciencedirect.com

Elsevier Masson France EM|consulte www.em-consulte.com

Review

State of the art on dose prescription, reporting and recording in Intensity-Modulated Radiation Therapy (ICRU report No. 83)

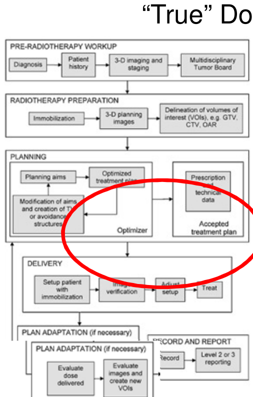
*Recommandations de l'ICRU sur la prescription, le rapport et l'enregistrement de la dose en radiothérapie avec modulation d'intensité (RCMI)*

V. Grégoire[a,*], T.R. Mackie[b]

[a] Center for Molecular Imaging and Experimental Radiotherapy & Radiation Oncology Department, Université catholique de Louvain, St-Luc University Hospital, avenue Hippocrate 10, 1200 Brussels, Belgium
[b] University of Wisconsin – Madison, Departments of Human Oncology, Medical Physics, 600 Highland Avenue, Madison WI 53792, USA

Gregoire, Cancer/Radiothérapie 15 (2011) 555–559

“True” Dose Reporting




**4. Dose-volume prescription, reporting and recordin**

- measurement of the intensity pattern from individual a specific patient;
- measurements of absorbed dose in a phantom of t intensity pattern planned for a specific patient;
- independent but equivalently accurate absorbed-dos tions for the patient specific beam intensity pattern;
- in vivo dosimetry.

Gregoire, Cancer/Radiothérapie 15 (2011) 555–559

## Delivery Variations / Adaptive RT – Anatomic Sites

| | |
|---|---|
| Head &Neck | Adaptive radiotherapy of head and neck cancer. Castadot et al. Semin Radiat Oncol. 20:84, 2010<br>Adaptive radiation therapy for head and neck cancer-can an old goal evolve into a new standard? Schwartz et al. J Oncol. 2011;2011. pii: 690595. Epub 2010 Aug 18. |
| Lung | Role of Adaptive Radiotherapy During Concomitant Chemoradiotherapy for Lung Cancer: Analysis of Data From A Prospective Clinical Trial. IJROBP. 75(4):1092-7, 2009<br>Potential of adaptive radiotherapy to escalate the radiation dose in combined radiochemotherapy for locally advanced non-small cell lung cancer. Guckenberger et al. IJROBP, 79, 901–908, 2011 |
| Bladder | Offline adaptive radiotherapy for bladder cancer using cone beam computed tomography. Foroudi et al. J Med Imaging Radiat Oncol. 2009;53(2):226-33. |
| Cervix | MRI assessment of cervical cancer for adaptive radiotherapy. Dimopoulos et al. Strahlenther Onkol. 2009;185(5):282-7. |

## Clinical Applications:
### Observing vs Reacting (Adaptive RT)

**Maintain initial plan integrity:**
Tumor Progression: ~10%
Dosimetric Variations: ~20-30%
Changing anatomy: e.g. Weight loss / Tumor response

**Change plan to benefit from response:**
Change occurring early enough to change plan: ~20%?

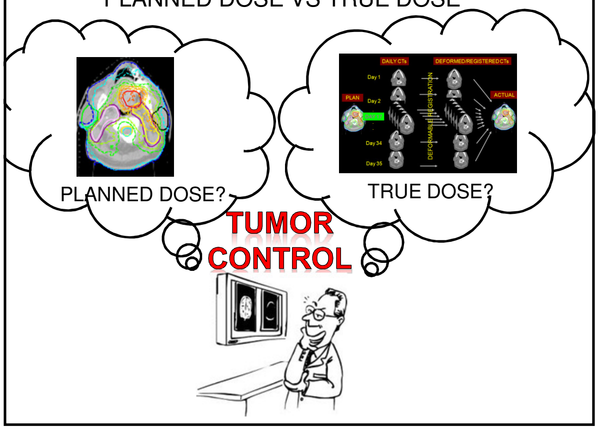
**FUTURE CLINICAL TRIALS: AIMS?**
- Maintain integrity: Head/Neck, esophagus, prostate?
- Benefit from response: Lung, Gliomas, GYN?

## IMPACT OF ANATOMIC VARIATIONS / ADAPTIVE RT CLINICAL QUESTIONS

- Types of cases and delivery techniques?
- Timing and techniques of dose assessments?
- Magnitude of dosimetric variation vs clinical impact?
- If adaptive, timing of replanning?
- Shrinking margins - Residual microscopic disease?
- Maintaining versus escalating doses?
- Cost effectiveness?

Clinical Scenarios

PLANNED DOSE VS TRUE DOSE




Local Control Assessment
vs
True Tumor Doses

**Tumor progression**
**Tumor response**
**Overall anatomic variations**

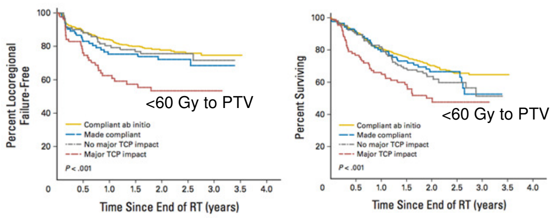
Clinical Contexts:
1. Head & Neck Ca: Toxic treatment
2. Lung Ca: Poor tumor control

VOLUME 28 · NUMBER 18 · JUNE 20 2010

JOURNAL OF CLINICAL ONCOLOGY | ORIGINAL REPORT

### Critical Impact of Radiotherapy Protocol Compliance and Quality in the Treatment of Advanced Head and Neck Cancer: Results From TROG 02.02

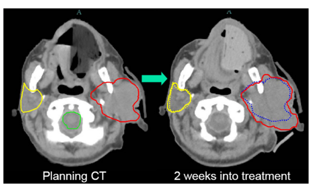
*Lester J. Peters, Brian O'Sullivan, Jordi Giralt, Thomas J. Fitzgerald, Andy Trotti, Jacques Bernier, Jean Bourhis, Kally Yuen, Richard Fisher, and Danny Rischin*




---

Adaptive RT: Clinical Observations

Maintaining the integrity of the initial delivery plan
**Tumor progression**




Lei Dong, MDACC

UM: 2/14 lung Ca patient progression
Feng et al, IJROBP, 73, 1228, 2009

VU: 1/21 lung Ca patients progression
Spoelstra et al, IJROBP, Vol. 75, 1092, 2009

---

## Head & Neck: Adaptive RT

- Duma *et al. Adaptive radiotherapy for soft tissue changes during helical tomotherapy for head and neck cancer. Strahlenther Onkol 2012.*
- Loo *et al. Tumour shrinkage and contour change during radiotherapy increase the dose to organs at risk but not the target volumes for head and neck cancer patients treated on the TomoTherapy HiArt system. Clin Oncol (R Coll Radiol) 2011;23:40-47.*
- You *et al. Is There a Clinical Benefit to Adaptive Planning During Tomotherapy in Patients with Head and Neck Cancer at Risk for Xerostomia? Am J Clin Oncol 2011.*
- Capelle *et al. Adaptive Radiotherapy Using Helical Tomotherapy for Head and Neck Cancer in Definitive and Postoperative Settings: Initial Results. Clin Oncol (R Coll Radiol) 2011.*
- Fung *et al.* Dosimetric evaluation of a three-phase adaptive radiotherapy for nasopharyngeal carcinoma using helical tomotherapy. *Med Dosim 2011.*
- Fiorino *et al. Introducing the Jacobian-volume-histogram of deforming organs: application to parotid shrinkage evaluation. Phys Med Biol 2011;56:3301-3312.*

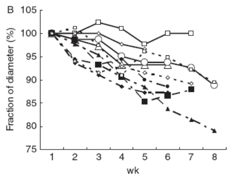
## Head & neck: True Dose Documentation

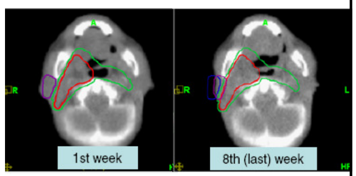
Yonsei University / Korea:

10 patients with weight loss or neck diameter decrease:
Higher rates of Grade 2 xerostomia

MVCTs were retrospectively contoured, 1 MVCT/week

Doses recalculated based on deformed MVCTs




You et al. Am J Clin Oncol 35(3):261-6, 2011.

## Head and Neck Ca:
## Adaptation with Functional Changes?

Dirix P et al. Dose painting in radiotherapy for head and neck squamous cell carcinoma: value of repeated functional imaging with (18)F-FDG PET, (18)F-fluoromisonidazole PET, diffusion-weighted MRI, and dynamic contrast-enhanced MRI. J Nucl Med 2009;50:1020–7.

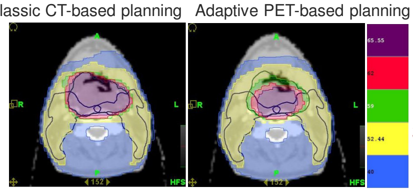
Madani I et al. Positron emission tomography-guided, focal-dose escalation using intensity-modulated radiotherapy for head and neck cancer. Int J Radiat Oncol Biol Phys 2007;68:126–35.

Geets X, Tomsej M, Lee JA, et al. Adaptive biological image-guided IMRT with anatomic and functional imaging in pharyngo-laryngeal tumors: impact on target volume delineation and dose distribution using helical tomotherapy. Radiother Oncol 2007;85:105–15.

Duprez F, De Neve W, De Gersem W, et al. Adaptive Dose Painting by Numbers for Head-and-Neck Cancer. Int J Radiat Oncol Biol Phys 2011; 80; 1045-55.

## Adaptive RT: Impact on dose distribution

Classic CT-based planning    Adaptive PET-based planning



SIB-IMRT
30x2.3 Gy
30x1.85 Gy

P<0.001

| Planning | $V_{10}$ | $V_{50}$ | $V_{80}$ | $V_{90}$ | $V_{95}$ | $V_{100}$ |
|---|---|---|---|---|---|---|
| *Classic CT-based* | 100% | 100% | 100% | 100% | 100% | 100% |
| *Adaptive CT-based* | 99% | 100% | 100% | 85% | 80% | 66% |
| *Classic PET-based* | 99% | 99% | 98% | 83% | 82% | 81% |
| *Adaptive PET-based* | 99% | 100% | 98% | 73% | 67% | 58% |

Courtesy Vincent Gregoire, 2010

Geets, Radiother Oncol 2007;85:105–15

**There is evidence that Adaptive Radiotherapy in Head and Neck cancer patients:**

1. will not benefit any patient, regardless of any endpoint (dosimetric or clinical).
2. will not benefit patients who show progression during radiotherapy.
3. might benefit a subset of patients who display tumor regression or significant weight loss.
4. should be performed on-line to be truly effective.
5. improves survival in nasopharyngeal cancers.

10

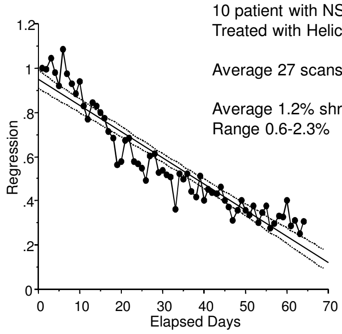
## Lung Ca: Tumor Regression – Anatomic Changes

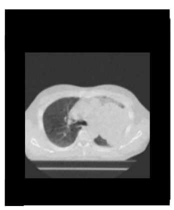
Kupelian et al., IJROBP, 2005

10 patient with NSCLC,
Treated with Helical Tomotherapy

Average 27 scans per patient

Average 1.2% shrinkage per day:
Range 0.6-2.3%



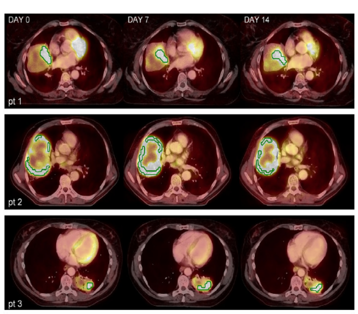
## Lung Ca: Functional Changes
## TARGETS OF ADAPTATION TO TUMOR RESPONSE

Aerts et al, IJROBP, Vol. 71, No. 5, pp. 1402–1407, 2008

N=23 patients
ST I-III NSCLC

VARYING VOLUMES
BUT
STABLE LOCATION:

SUITABLE
TARGETS FOR
ADAPTATION



**FDG-PET scans might provide attractive targets for adaptive radiotherapy in lung cancer because:**

1. they mostly display changes in volume but not location.
2. they mostly display changes in location but not volume.
3. FDG-PET scans are routinely obtained throughout a course of radiotherapy.
4. auto-contouring is possible by SUV values on FDG-PET scans.
5. they have been shown to reveal areas of future in-field recurrences.

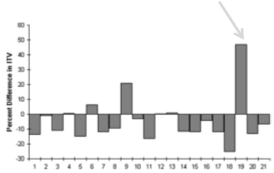
10

Clinical Application:
Change plan to benefit from response

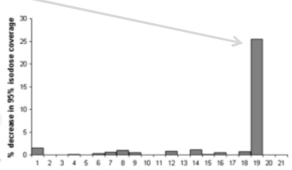
LUNG CANCERS

ADAPTIVE RT:
NOT FOR EVERY PATIENT
NOT FOR EVERY TECHNIQUE

N=21 evaluable patients
8% reduction after 30 Gy
Only patient needing replan had progression…




Volume Change after 30 Gy




Dosimetric miss after 30 Gy

Spoelstra et al, IJROBP, Vol. 75, 1092, 2009

PHYSICS CONTRIBUTION

**ADAPTIVE RADIOTHERAPY PLANNING ON DECREASING GROSS TUMOR VOLUMES AS SEEN ON MEGAVOLTAGE COMPUTED TOMOGRAPHY IMAGES**

CURTIS WOODFORD,* SLAV YARTSEV, PH.D.,* A. RASHID DAR, M.D.,*† GLENN BAUMAN, M.D.,*† AND JAKE VAN DYK, M.SC.*†

*London Regional Cancer Program, London Health Sciences Centre, London, Ontario, Canada; and †The University of Western Ontario, London, Ontario, Canada

17 lung Ca Cases. RT ~30 fractions.

In **40%** of patients in this study, GTV changes were of sufficient magnitude and occurred sufficiently early in the treatment course that one could realistically anticipate that adapted radiotherapy would improve the therapeutic ratio.

If GTV decreases by greater than 30% at any point in the **first 20 fractions of treatment**, adaptive planning is appropriate to further improve the therapeutic ratio.

Woodford et al, IJROBP 69, p 1316, 2007

PHYSICS CONTRIBUTION

**USING FLUORODEOXYGLUCOSE POSITRON EMISSION TOMOGRAPHY TO ASSESS TUMOR VOLUME DURING RADIOTHERAPY FOR NON–SMALL-CELL LUNG CANCER AND ITS POTENTIAL IMPACT ON ADAPTIVE DOSE ESCALATION AND NORMAL TISSUE SPARING**

MARY FENG, M.D.,* FENG-MING KONG, M.D., PH.D.,* MILTON GROSS, M.D.,† SHANELI FERNANDO, M.D.,* JAMES A. HAYMAN, M.D.,* AND RANDALL K. TEN HAKEN, PH.D.*

Departments of *Radiation Oncology, and †Nuclear Medicine, University of Michigan, Ann Arbor, MI

Mid-RT PET volumes were used to design boost fields.

N=14 Complete CR in 2 patients
Progression by PET in 2 patients

Mid-RT PET in remaining 10 patients:
Mean decrease in PET volumes: 44% range 10-100%

RT boosts could be designed in the **10/14** patients to increase doses above 100 Gy and reduce normal tissue complication probablities.

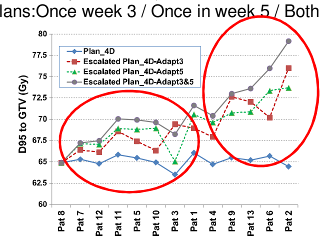
Feng et al, IJROBP, 73, 1228, 2009

## Adaptive RT; Dose Escalation – Lung Ca

University of Wuerzburg, Guckenberger et al. IJROBP, 79, 901, 2011

N=13 patients, advanced NSCLC, weekly CT images
Dose accumulation performed (Surface-based DIR algorithm)
Adaptive plans:Once week 3 / Once in week 5 / Both in weeks 3 then 5

**Results;**




Safe dose escalation **on average** from 66 Gy to 74 Gy in all patients

1. **Adaptive RT failed in some patients**
2. **Dose escalation to ~74 Gy was possible in some patients**

# FUTURE CLINICAL TRIALS?

## Adaptive RT; Dose Escalation / Lung Ca – RTOG 1106

**RADIATION THERAPY ONCOLOGY GROUP**
**American College of Radiology Imaging Network**

**RTOG 1106/ACRIN 6697**

**RANDOMIZED PHASE II TRIAL OF INDIVIDUALIZED ADAPTIVE RADIOTHERAPY USING DURING-TREATMENT FDG-PET/CT AND MODERN TECHNOLOGY IN LOCALLY ADVANCED NON-SMALL CELL LUNG CANCER (NSCLC)**


**Principal Investigator**
Radiation Oncology/Translational Research
Feng-Ming (Spring) Kong, MD, PhD
University of Michigan
1500 E. Medical Center Dr./UH B2 C490, SPC 5010
Ann Arbor, MI 48109
734-936-7810/FAX 734-763-7370
fengkong@umich.edu


| STRATIFY | | RANDOMIZE[3] | |
|---|---|---|---|
| | **MLD**<br>1. >14 Gy<br>2. ≤ 14 Gy<br><br>**PreGTV**<br>1. ≥ 200 cc<br>2. < 200 cc<br><br>**Histology**<br>1. Squamous<br>2. Non-Squamous | | **Arm 1: Concurrent Chemoradiotherapy**<br>RT to 50 Gy in 25 fractions in 5 weeks<br>[4]Carboplatin and paclitaxel weekly<br><br>**Arm 2: Concurrent Chemoradiotherapy**<br>RT to 47.5-49.5 Gy in 17-22 fractions in 3-4 weeks<br>[4]Carboplatin and paclitaxel weekly |

**ALL PATIENTS: During-RT FDG-PET/CT Scan**

**Arm 1:** At fraction 20-23 (weeks 4-4.5)

**Arm 2:** At fraction ~14-21 (weeks 3-4)

**Arm 1:** Continuation of radiotherapy, not based on during-RT FDG-PET/CT scan with carboplatin and paclitaxel for a total of 6 weekly cycles

10 Gy in 5 fractions; overall total of 60 Gy in 30 daily fractions in 6 weeks

**Arm 2:** Adaptive radiotherapy, based on during-RT FDG-PET/CT scan with carboplatin and paclitaxel for a total of 6 weekly cycles

34-37.8 Gy in 8-13 fractions; overall total of up to 85.5 Gy in 30 daily fractions in 6 weeks
Individualized to MLD 20 Gy

**ALL PATIENTS: Consolidative Chemotherapy**

**Arms 1 and 2:** Carboplatin and paclitaxel q21 days X 3

**IGRT is mandatory for this study (see Section 5.1).**

N=138

# Personalized RT prescriptions

**Table 6.1.2a: Individualized Doses and Fraction Sizes for Arm 2 (Based on 74 Gy Screening Plan)**

| | (1) Mean Lung Dose for the screening plan (74 Gy PTV dose) | (2) Initial Dose per fx (Gy) | (3) # Fractions for ~50 Gy EQD2 Tumor Dose | (4) Physical Dose at this time point (Gy) | (5) Minimum # Fractions Before 2nd PET scan | (6) Adaptive Phase Largest allowed Boost Dose per fx (Gy) | (7) Adaptive Phase # of Fractions | (8) Adaptive Phase Largest allowed Physical Boost Dose (Gy) | (9) Largest allowed Total Physical Prescription Dose (Gy) |
|---|---|---|---|---|---|---|---|---|---|
| a) | <13.5 | 2.85 | 17 | 48.45 | 14 | 2.85 | 13 | 37.05 | 85.5 |
| b) | 13.5 | 2.85 | 17 | 48.45 | 14 | 2.85 | 13 | 37.05 | 85.5 |
| c) | 13.9 | 2.80 | 17 | 47.6 | 14 | 2.9 | 13 | 37.7 | 85.3 |
| d) | 14.3 | 2.75 | 18 | 49.5 | 15 | 3 | 12 | 36 | 85.5 |
| e) | 14.7 | 2.70 | 18 | 48.6 | 15 | 3.05 | 12 | 36.6 | 85.2 |
| f) | 15.1 | 2.65 | 18 | 47.7 | 15 | 3.15 | 12 | 37.8 | 85.5 |
| g) | 15.5 | 2.60 | 19 | 49.4 | 16 | 3.25 | 11 | 35.75 | 85.2 |
| h) | 16.0 | 2.55 | 19 | 48.45 | 16 | 3.3 | 11 | 36.3 | 84.8 |
| i) | 16.5 | 2.50 | 19 | 47.5 | 16 | 3.4 | 11 | 37.4 | 84.9 |
| j) | 17.0 | 2.45 | 20 | 49 | 17 | 3.55 | 10 | 35.5 | 84.5 |
| k) | 17.6 | 2.40 | 20 | 48 | 17 | 3.65 | 10 | 36.5 | 84.5 |
| l) | 18.1 | 2.35 | 21 | 49.35 | 18 | 3.85 | 9 | 34.65 | 84.0 |

Keep total 30 fractions:
Largest fraction size allowed: 3.85 Gy

## Ablative doses in Locally Advanced Lung Cancer?

## An Adaptive RT application

Conventional dose escalation ineffective in advanced lung Ca:
RTOG 0617:
No difference 60 Gy vs 74 Fy

## SBRT Boost to Residual Disease

Feddock J et al. IJROBP, 78, S108, 2010
ASTRO 2010

PET-CT one month following conventional CRT

PET positive residual disease ($\leq$7 cm)
An additional 20 Gy in 2 SBRT fractions in 1 week.

N=19.
Median time interval from CRT to SBRT boost : 2 months.

Median follow-up time: 11 months
1 patient experienced grade 3 radiation pneumonitis (5%).

### Image-Guided Hypofractionated Radiotherapy with Stereotactic Boost and Chemotherapy for Inoperable Stage II-III Non-Small Cell Lung Cancer Phase I/II Protocol (UCLA) - PI: Percy Lee

**PET-CT**, 4D CT Simulation

↓

4 Gy x 10 fractions Involved Field RT

↓

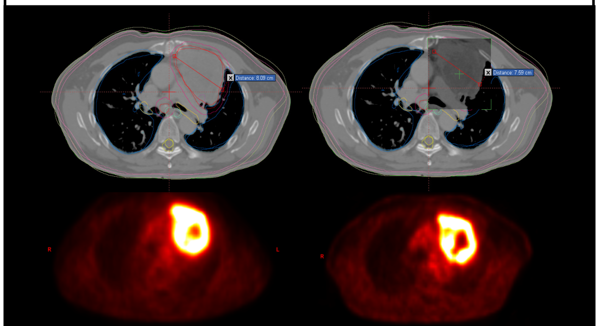
**PET-CT**, 4D CT Re-Simulation / **Adaptation**
(at the $8^{th}$ or $9^{th}$ fraction)

Dose-escalation cohorts: SBRT Boosts

5 Gy x 5 (N=15) or 6 Gy x 5 (N=15) or 7 Gy x 5 (N=15)

**3 WEEK COURSE**

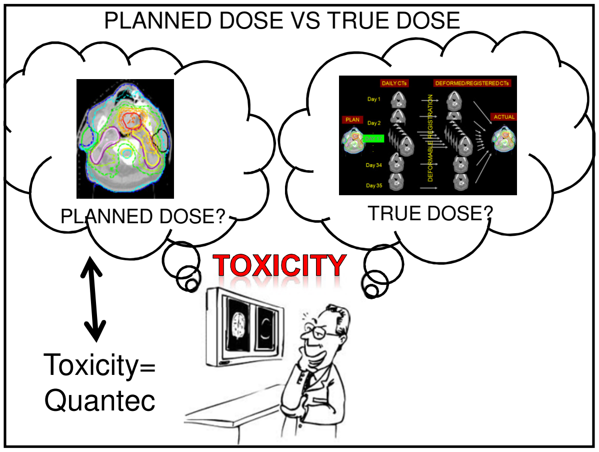
## Image-Guided Hypofractionated Radiotherapy with Stereotactic Boost and Chemotherapy for Inoperable Stage II-III Non-Small Cell Lung Cancer



Prior to RT

After 40 Gy in 10 Fractions

## PLANNED DOSE VS TRUE DOSE




## CLINICAL IMPLICATIONS: TOXICITY EVALUATIONS QUANTEC

(Quantitative Analysis of Normal Tissue Effects in the Clinic)


IJROBP, Vol. 76, No. 3, Supplement

Toxicity Assessment
vs
True Tumor Doses

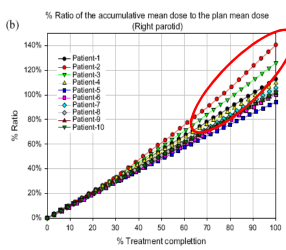
**Anatomic variations of organs at risk**

Clinical Context: Head & Neck Ca

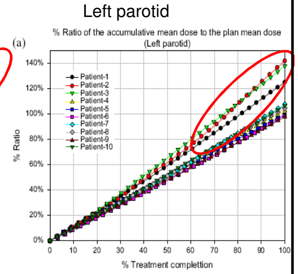
## Parotids can get hot in some patients

Deformable registration and dose accumulation on MVCTs
Lee at al. IJROBP 71, 1563-71, 2008

Right parotid




Left parotid

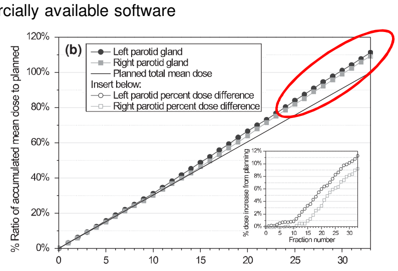



Overdose: Average= 15 %
3 of 10 patients: >10% higher mean parotid dose
7 of 10 patients: <10% (6-8%)

## Parotids can get hot in some patients

Deformable registration and dose accumulation on CBCTs
Elstrom et al. Acta Oncologica, 2010; 49: 1101–1108

Single case, 33 CBCTs: Deformation, dose accumulation.
Commercially available software



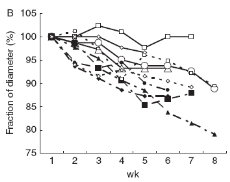
# Head & neck: Adaptive

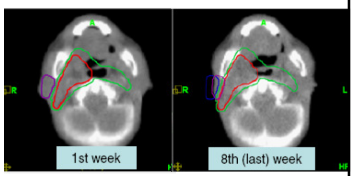
Yonsei University / Korea:

10 patients with weight loss or neck diameter decrease during H&N treatment: higher rates of Grade 2 xerostomia

MVCTs were retrospectively contoured, 1 MVCT/week

Planned Adaptive; recalculate dose based on deformed MVCTs




You et al. Am J Clin Oncol 35(3):261-6, 2011.

Clinical Oncology 24 (2012) 208–215

Contents lists available at SciVerse ScienceDirect

Clinical Oncology

journal homepage: www.clinicaloncologyonline.net

ELSEVIER

Original Article

**Adaptive Radiotherapy Using Helical Tomotherapy for Head and Neck Cancer in Definitive and Postoperative Settings: Initial Results**

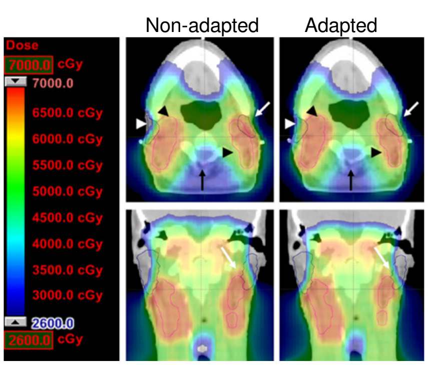
L. Capelle *, M. Mackenzie †, C. Field ‡, M. Parliament *, S. Ghosh ‡, R. Scrimger *

* Division of Radiation Oncology, Cross Cancer Institute, Edmonton, Canada
† Division of Medical Physics, Cross Cancer Institute, Edmonton, Canada
‡ Division of Experimental Oncology, Cross Cancer Institute, Edmonton, Canada

20 head and neck cancer patients:
All treated in 30 fractions
Replan after fraction #15
Start second plan with fraction #20

The two plans were added assuming first 19 fractions identical (plan 1) and last 11 fractions identical (plan 2)

# Adaptive Radiotherapy in Head and Neck Ca




Capelle et al. Clinical Oncology, 24 (2012) 208-215

## Adaptive Radiotherapy in Head and Neck Ca

- No benefit in patients treated postoperatively.
- In patients treated definitively:

1. Reduction in mean parotid dose
2. Reduction in normal tissue volume outside PTV >50 Gy
3. Patients with the following had the greatest benefit:
   Nasopharyngeal carcinoma patients
   Initial stage T3/4
   Weight loss
   Reduction in lateral neck separation

- Safety of adaptive approach:
  No evidence of in-field or marginal failures

Capelle et al. Clinical Oncology, 24 (2012) 208-215

**During a course of head and neck radiotherapy, daily parotid doses are expected to:**

1. remain constant in all patients, since daily positioning variations do not occur in a face mask.
2. increase in all cases, since parotid glands swell during radiotherapy.
3. increase whenever parotid glands migrate medially due patient weight loss and/or tumor regression.
4. increase in all cases, since all head and neck cancer patients invariably lose weight during treatment.
5. decrease in all cases, since all head and neck cancer patients invariably lose weight during treatment.

10

Adaptive Dose Painting in Head and Neck Cancer

An Adaptive RT application

Int. J. Radiation Oncology Biol. Phys., Vol. 80, No. 4, pp. 1045–1055, 2011

0360-3016/$–see front matter

ELSEVIER

doi:10.1016/j.ijrobp.2010.03.028

**CLINICAL INVESTIGATION** **Head and Neck**

**ADAPTIVE DOSE PAINTING BY NUMBERS FOR HEAD-AND-NECK CANCER**

Fréderic Duprez, M.D., Wilfried De Neve, M.D., Ph.D., Werner De Gersem, Ir., Ph.D., Marc Coghe, Lic, and Indira Madani, M.D., Ph.D.

Department of Radiotherapy, Ghent University Hospital, Ghent, Belgium

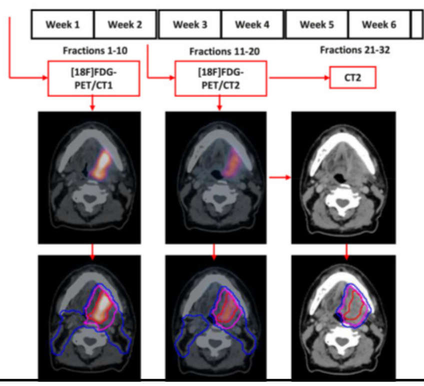
21 non-metastatic SCC Head and Neck
3 separate plans

Phase I; 2 dose levels – RT Alone (no chemotherapy)

| | | |
|---|---|---|
| Median doses: | 80.9 Gy to CTV | N=7 |
| | 85.9 Gy to GTV (smaller) | N=14 |

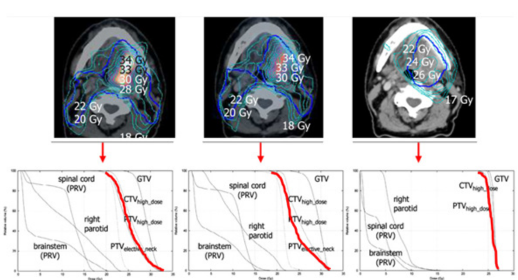
ADAPTIVE DOSE PAINTING

Duprez F et al.IJROBP, 2011; 80; 1045-55.




**ADAPTIVE DOSE PAINTING: HETEROGENEOUS DOSE ESCALATION**

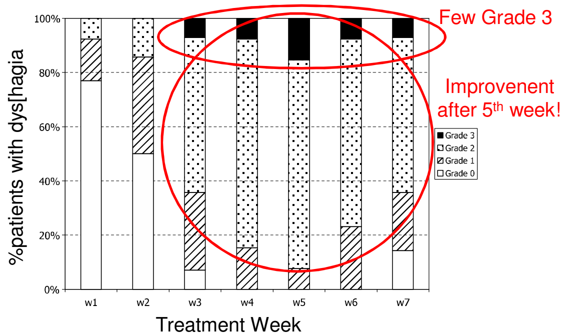
Duprez F et al.IJROBP, 2011; 80; 1045-55.



**ADAPTIVE DOSE PAINTING: LESS TOXICITY?**

Duprez F et al.IJROBP, 2011; 80; 1045-55.

ACUTE DYSPHAGIA – DOSE GROUP II (Dose 85.9 Gy, Target = GTV)




Evolution of Adaptive Radiotherapy

**Real-Time Radiotherapy**

**Daily On-line Adaptation**

**Triggered On-line Adaptation**

**Planned Off-line Adaptation**

**Triggered Off-line Adaptation**

**No adaptation**

# Real-Time Radiotherapy

Assessment and adjustments:

- Daily (all fractions)
- On-line
- Intra-fraction variations included
- Deformable registration
- Dose accumulation (inter/intrafraction)
- Real-time adaptation

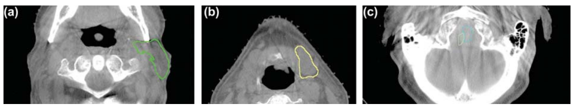
## Complexity of Process: ?On-line evaluation / adaptive
Deformation / Dose accumulation / CBCTs

Elstrom et al. Acta Oncologica, 2010; 49: 1101–1108

Single case, 33 CBCTs: Deformation, dose accumulation.
Commercially available software

165 contours evaluated: 33% good
77% acceptable

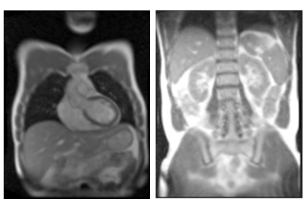
~45 minutes to “prepare” each fraction, not counting verification by MD
Off-line an option
On-line would be too inefficient




## Real-Time Radiotherapy: In-room MRI

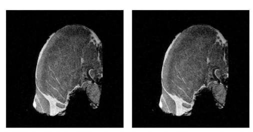
Inter/Intrafraction motion/deformation assessment

In-room MRI / Cobalt IMRT



(not approved for clinical use)

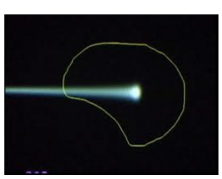
In-room MRI / Linac

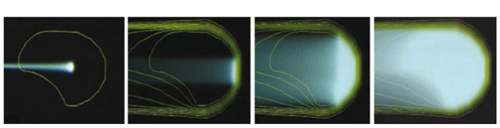


Phys Med Biol. 2009 Jun 21;54(12):N229-37
Phys Med Biol. 2009 Sep 21;54(18):N409-15

(not approved for clinical use)

## Real-Time Radiotherapy: A necessity for IMPT?



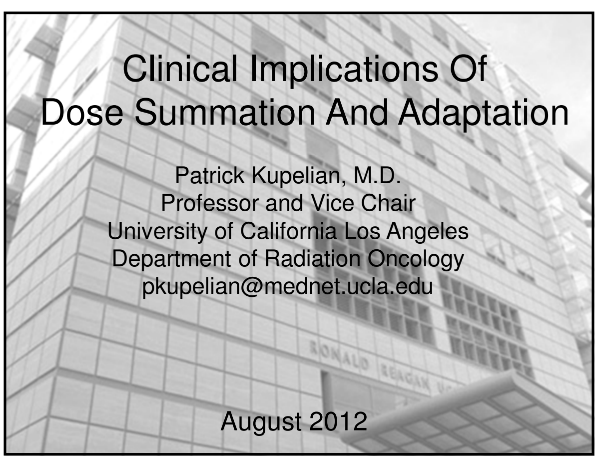


## Dose Summation And Adaptation Conclusions

- Modern in-room imaging techniques enable documentation of anatomic and dosimetric variations throughout treatment courses.
- Deformable registration and dose accumulation allow determination of “true” delivered dose versus planned dose.
- Clinical correlations previously made with “planned” doses should be reassessed with “true” delivered doses.

## Dose Summation And Adaptation Conclusions

- Adaptive Radiotherapy is a process that addresses deforming anatomy, allowing robustness of planned delivery and possibly enabling dose escalation whenever appropriate.
- The proportion of patients benefiting from Adaptive RT still unclear (10-40%?)…
- Future design of treatment protocols within or outside of clinical trials whould include mecahnisms to document “true” delivered doses.
- Tools are still to be refined.



# Clinical Implications Of Dose Summation And Adaptation


Patrick Kupelian, M.D.
Professor and Vice Chair
University of California Los Angeles
Department of Radiation Oncology
pkupelian@mednet.ucla.edu


August 2012