The Critical Importance of High Quality in Radiation Therapy

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Making Cancer History®

Quality in Radiation Therapy

- Radiation therapy is versatile and important for many patients
- Intuitively, quality is very important
  - Get the right dose to the right place
- Achieving optimal quality can be challenging

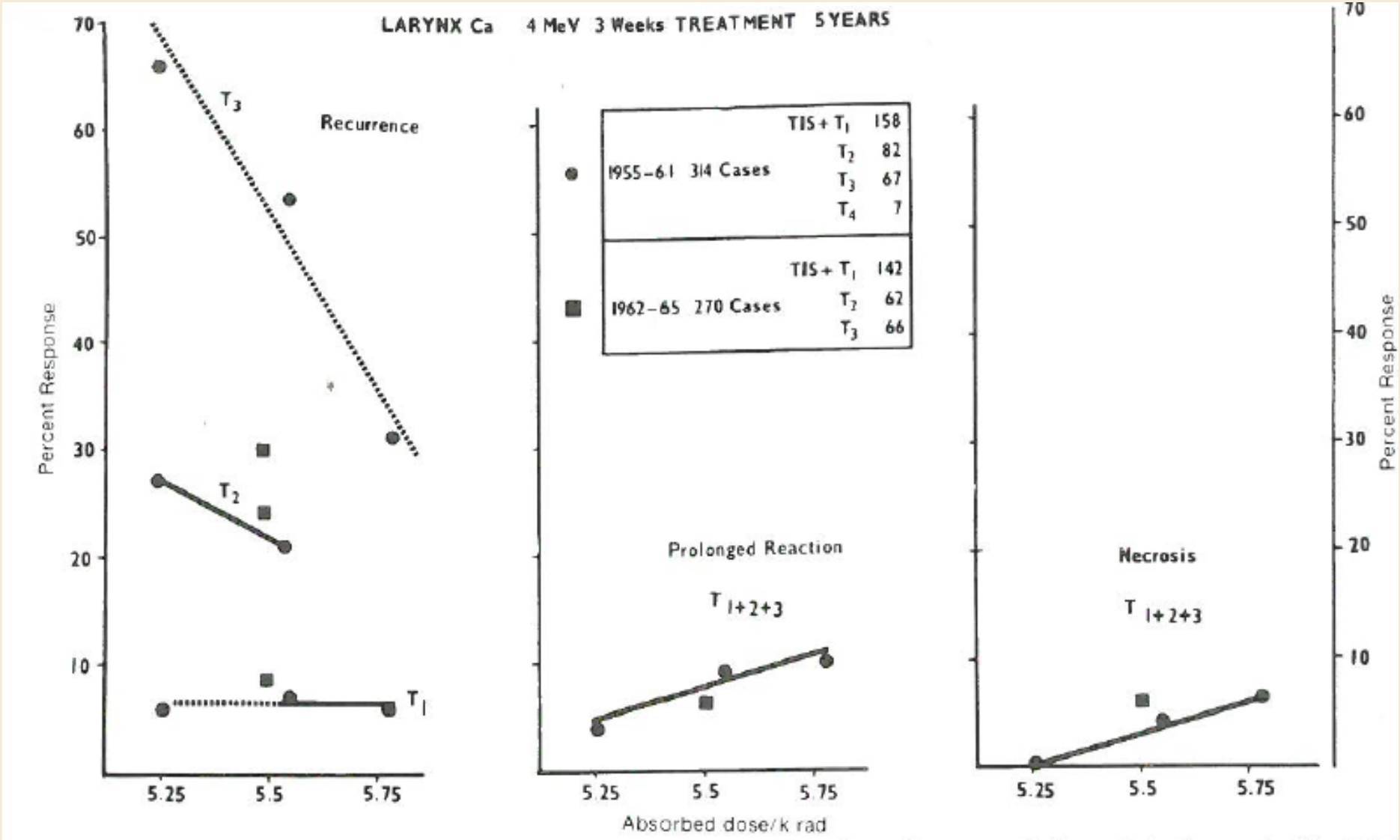
- Introduction to these sessions:
  - What accuracy is needed in RT?
  - How important is good quality?

What accuracy is necessary?

- What is the right dose?
  - How right is “right”?

- ICRU Report 24 (1976)
  - “…the available evidence… points to the need for an accuracy of +/- 5% in the deliver of an absorbed dose to a target volume if the eradication of the primary tumor is sought.”
  - Biological variability in an endpoint is <5%

Underlying ICRU data



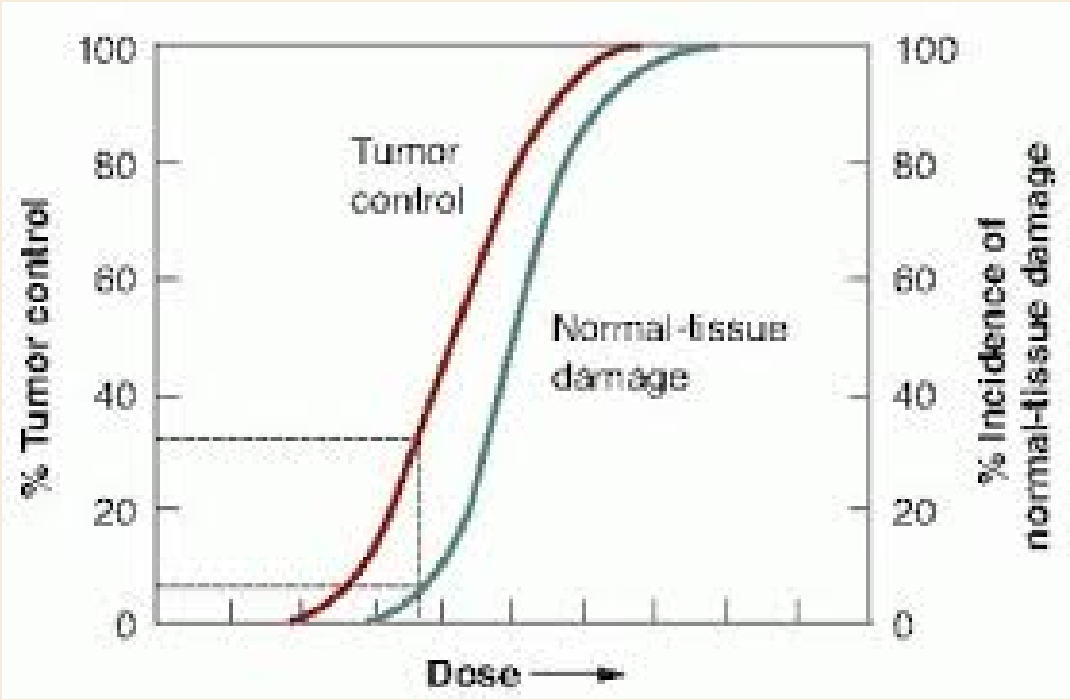
Further evidence:

- Tumor control: Randomized photon vs electron treatment
  - Same nominal dose, but significantly poorer tumor control with electrons
  - Turned out there was a 7%-low calibration error in the electrons
- Normal tissue complication: GYN reactions
  - Excessive GI and skin reactions observed
  - Investigation identified a 7-10%-high output calibration error
  - Other patients did not show errors

- Reported in Dutreix Radiother Oncol 1984

Dose response

- Variations make sense in terms of basic dose response biology
- Sensitivity depends on where we are on the dose response curve
  - if we are on the shoulder, not as sensitive
- Usually we're somewhere on this slope and therefore sensitive to dose variations



Further consideration

- 5% is the total uncertainty
- There are many components that make up this uncertainty budget
  - Uncertainty in individual components must be much less
- Dose calculation: 2% is often quoted
  - AAPM TG-65 report: Tissue inhomogeneity corrections for megavoltage photon beams.

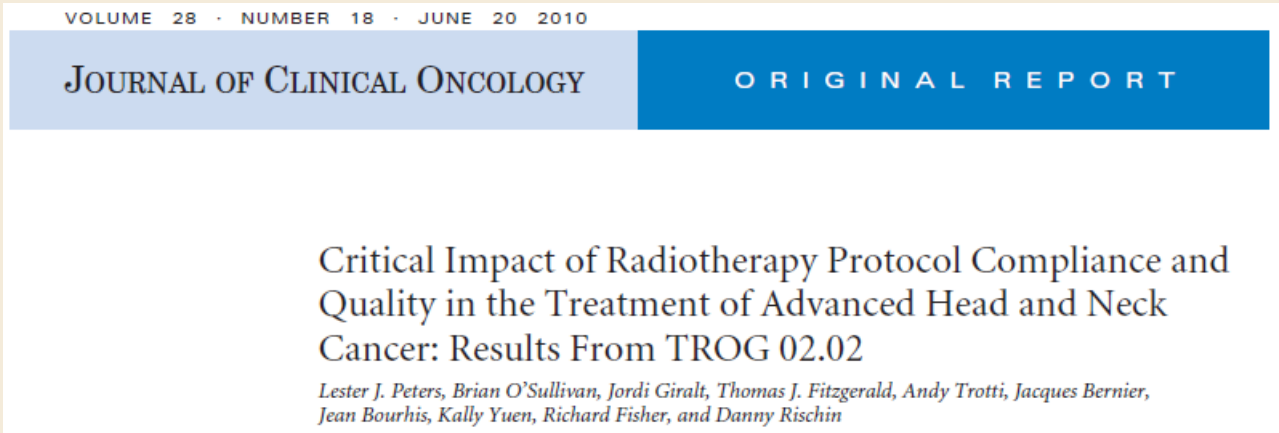
How important is good quality?

- We need to be within 5%
- Previous slides showed observable effects from very specific conditions of dose variation

- What about the bigger question of how quality affects radiotherapy outcomes in contemporary RT?

A contemporary example: TROG 02.02

- Cisplatin (CIS) vs Cisplatin + tirapazamine (TPZ)
- All patients: 70 Gy in 35 fx using a shrinking field technique
- Hypothesis: 10% improvement in 2 year overall survival
- 861 patients



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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

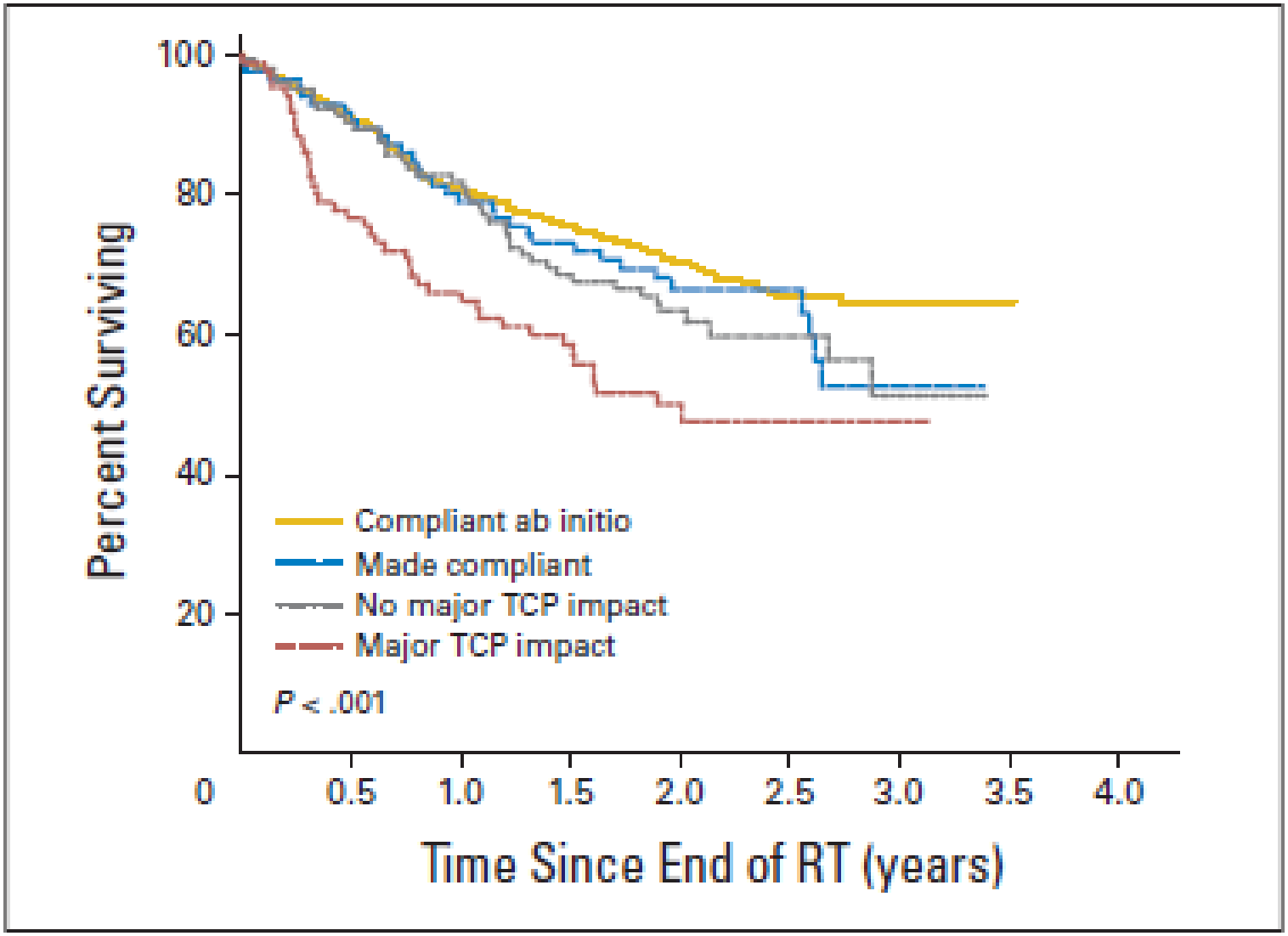
RT Quality

- Quality assessed in terms of protocol compliance: delivering standard of care.
- Correct RT from outset (n=502)
- RT corrected during tx (n=86)
  - Median <10 treatment days to finalize changes
- RT not correct, but not expected to have major impact (n=105)
- RT not correct, expected to have major impact (n=97)

What is the nature of RT errors?

- 97 RT cases were deficient and expected to cause outcome problems
  - Inadequate planning/coverage (41)
  - Incorrect dose prescription (25)
  - Incorrect target definition (24)
  - Excessively prolonged treatment (7)
- Inadequate dose or missing the target
- Based on plan, but equivalent to
  - Poor beam model that overestimates dose
  - Miscalibrated beam
  - Incorrect alignment

How important is it?



2 year overall survival: 70% vs 50%

Put into perspective

- Justification for this multimillion dollar phase 3 clinical trial was:
- A hypothesized 10% improvement in 2 y overall survival!
- Versus a 20% difference based on the quality of RT!!

- The quality of RT is critical to patient survival

Follow-up to 02.02

“The impact of radiotherapy quality on treatment outcome would likely increase with the introduction and increasing use of more advanced radiotherapy techniques, such as intensity-modulated radiation therapy and stereotactic radiotherapy”

Editorials

More Lessons Learned From the Suffocation of Hypoxia

K. Kian Ang, *The University of Texas M. D. Anderson Cancer Center, Houston, TX*

This pattern persists

- Protocol compliance as surrogate for RT quality
- Poorer protocol compliance leads to poorer outcomes
  - Poorer tumor control
  - Poorer survival
- Outcomes for patients who received the protocol treatment vs. those with >5-10% dose deviations

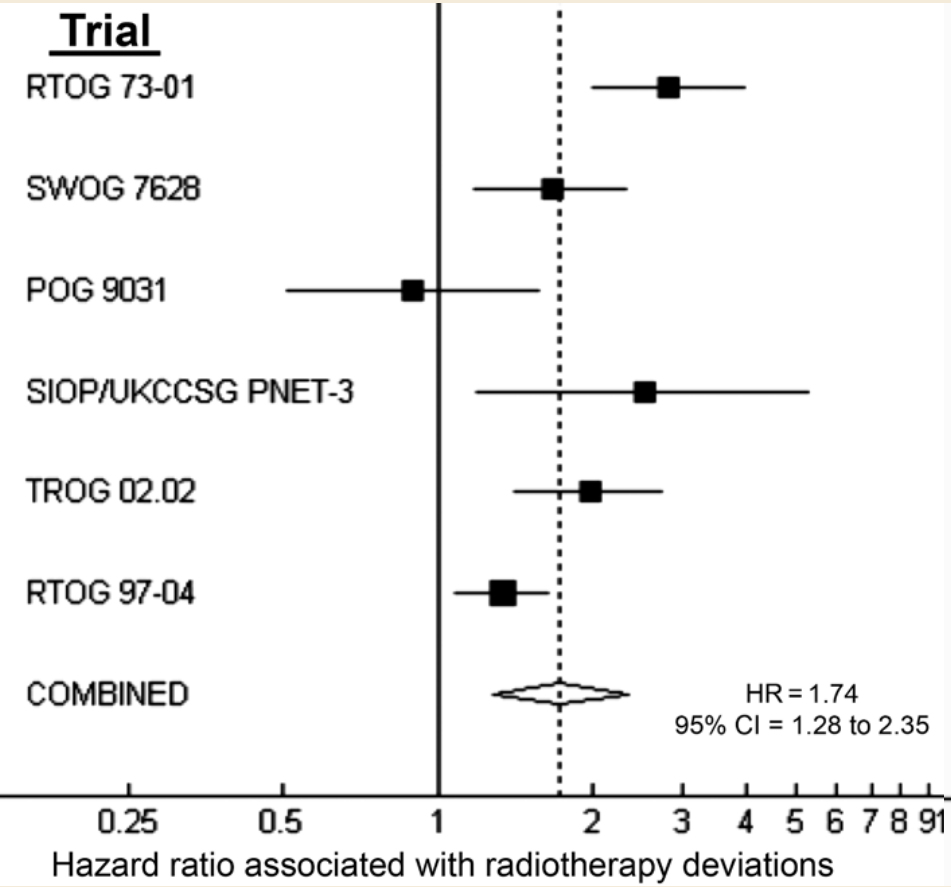
Radiotherapy Protocol Deviations and Clinical Outcomes: A Meta-analysis of Cooperative Group Clinical Trials

Nitin Ohri, Xinglei Shen, Adam P. Dicker, Laura A. Doyle, Amy S. Harrison, Timothy N. Showalter

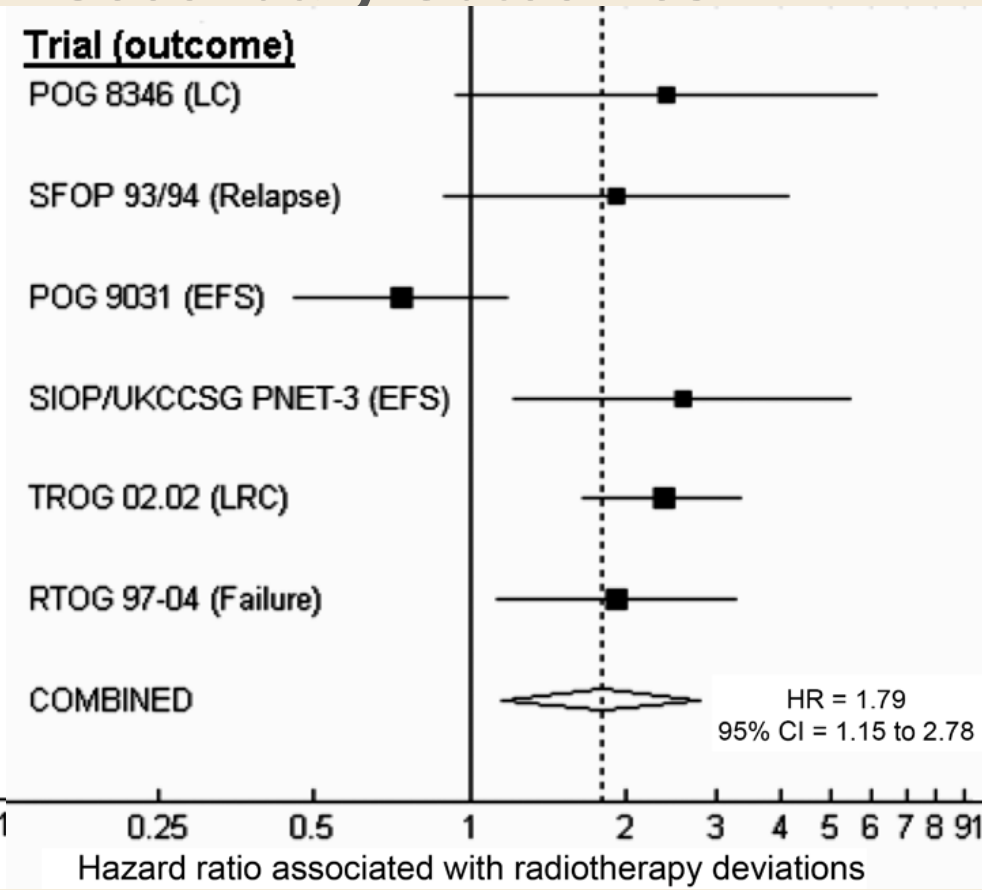
Manuscript received August 13, 2012; revised November 27, 2012; accepted November 27, 2012.

Protocol compliance summary:

Hazard ratio for Overall Survival



Hazard ratio for Secondary Outcomes



Failure to give an optimal dose leads to poorer outcomes

Summary

- For many tumors and side effects, we need to be within ~5%
  - Need to be within 2% for dose calculation
- If we don’t achieve that, we dramatically compromise patient outcomes
  - Overall survival substantially reduced when quality is not adequate

But there's more

- Radiotherapy practice is based on evidence
- Evidence comes from clinical trials
  - gold standard
- Low quality undermines these trials; no answer
  - risk obscuring discovery of optimal treatments, and progression and innovation

- **Consider these points when audit results are presented**

End

1. AAPM TG-65 report: Tissue Inhomogeneity corrections for megavoltage photon beams. 2004.
2. Ang K. More lessons learned from the suffocation of hypoxia. J Clin Oncol.
3. Dutreix A. When and howe can we improve precision in radiotherapy? Radiother Oncol 2:275-292; 1984.
4. ICRU report 24: Determination of absorbed dose in a patient irradiated by beams of x or gamma rays in radiotherapy. 1976.
5. Ohri N, Shen X, Dicker AP, et al. Radiotherapy protocol deviations and clinical outcomes: a meta-analysis of cooperative group clinical trials. J Natl Cancer Inst. 105:387-393; 2013
6. Peters LJ, O'Sullivan BO, Giralt J, et al. Critical Impact of radiotherapy protocol compliance and quality in the treatment of advanced head and neck cancer: results from TROG 02.02. J Clin Oncol. 28:2996-3001; 2010