Conflict of Interest

Dr. Grimm designed and holds intellectual property rights to the DVH Evaluator software tool (www.DiversiLabs.com) which is an FDA-cleared product in commercial use, and which has been used for this analysis.

Funding from Accuray, NovoCare

25 Years of SBRT


Why are there so few late effects?

Why does SBRT work so well?

HyTEC:

Goals like QUANTEC for SBRT

QUANTEC: Quantitative Analyses of Normal Tissue Effects in the Clinic

HyTEC: High Dose per Fraction, Hypofractionated Treatment Effects in the Clinic

SBRT: Stereotactic Body Radiation Therapy

QUANTITATIVE ANALYSES OF NORMAL TISSUE EFFECTS IN THE CLINIC

Guest Editors: Lawrence R. Marks, M.D.  Randall E. Ten Haken, Ph.D.  Mary K. Markel, Ph.D.
Today’s Session:

**Rationale and Evidence for SBRT**

a.k.a. Why does SBRT work so well?

**HyTEC Vision Papers: Rationale and Evidence for SBRT**

- Not easy to achieve high local control rates for lung tumors

  Fowler JF, Tomé WA, Fenwick JD, Mehta MP
  A challenge to traditional radiation oncology
  Int J Radiat Oncol Biol Phys.
  2004 Nov 15;60(4):1241-56
A pooled analysis of biological equivalent dose and local control, Stage 1 lung cancer

- About 1000 conventional cases...
  - Mehta N, King CR, Agazaryan N, Stranberg M, Hua A, Lee P
  - Stereotactic body radiation therapy and 3-dimensional conformal radiotherapy for stage I non-small cell lung cancer: A pooled analysis of biological equivalent dose and local control.

- About 1500 SBRT cases...
  - Mehta N, King CR, Agazaryan N, Stranberg M, Hua A, Lee P
  - Stereotactic body radiation therapy and 3-dimensional conformal radiotherapy for stage I non-small cell lung cancer: A pooled analysis of biological equivalent dose and local control.

- About 2500 pooled cases...
  - Mehta N, King CR, Agazaryan N, Stranberg M, Hua A, Lee P
  - Stereotactic body radiation therapy and 3-dimensional conformal radiotherapy for stage I non-small cell lung cancer: A pooled analysis of biological equivalent dose and local control.
A pooled analysis of biological equivalent dose and local control, Stage 1 lung cancer

Dr. Percy Lee's group at UCLA

- Logistic Model, Linear Quadratic (LQ), α/β=8.6Gy...
- Mehta N, King CR, Agazaryan N, Steinberg M, Hua A, Lee P
- Stereotactic body radiation therapy and 3-dimensional conformal radiotherapy for stage I non-small cell lung cancer: A pooled analysis of biological equivalent dose and local control.

95% 2 Year Local Control

- USC: 151.1 Gy BED_{1.6} = 22.6Gy x 3 fractions
- LQ: 192.9 Gy BED_{1.6} = 19.6Gy x 3 fractions
  ≈ 20Gy x 3 fractions
  Physical dose

95% Local Control may be achievable!!!

- Mehta N, King CR, Agazaryan N, Steinberg M, Hua A, Lee P
- Stereotactic body radiation therapy and 3-dimensional conformal radiotherapy for stage I non-small cell lung cancer: A pooled analysis of biological equivalent dose and local control.

95% Local Control may be achievable!!!

- Mehta N, King CR, Agazaryan N, Steinberg M, Hua A, Lee P
- Stereotactic body radiation therapy and 3-dimensional conformal radiotherapy for stage I non-small cell lung cancer: A pooled analysis of biological equivalent dose and local control.
For NSCLC, then, it follows that there is no need to invoke a "new biology" to explain the high tumor control rates.

We disagree, however, that the data presented can support this conclusion.

clearly demonstrate that secondary cell death that is most likely caused by deterioration of the tumor physiology is involved in the response of tumors to high dose per-fraction SRS and SBRT.

Is Indirect Cell Death Involved in Response of Tumors to Stereotactic Radiosurgery and Stereotactic Body Radiation Therapy?

http://dx.doi.org/10.1097/HOR.0b013e31820e0257
Dear Joe, Mike, Jimm,

You've probably seen this already? Rad Res 2012;177:311–327. This new paper, by Chan Song, has the best discussion re high dose-per-fraction that I have ever seen, with his conclusion in Fig 7. I’ll try and attach the pdf to this e-mail, but the copyright mechanisms might defeat me, so I put the actual ref first. do Please read the text! Best - Jack

The main advocate for the LQ model, showing interest in vascular damage!

Rad Res 2012;177: 311-327

FIG. 7. Hypothetical cell death mechanism in the tumor.

The main advocate for the LQ model, showing interest in vascular damage!

From: Jimm Grimm
Date: Thu, 19 Jun 2014 18:28:29 -0700
To: WGSBRT
Subject: Re: Very interesting article: response to Brown

Hi!

The MSKCC editorial is in the July issue of Rad Journal – see attached - with a reply by Brown, Carlson, and Brenner.

To me the irony is that by declaring ‘there is no need to invoke a “new biology” to explain the high tumor control rates,’ Brown et al. have sparked so much interest in studying that new biology.

The total number of photons delivered is generally lower in SBRT than in conventional fractionation and many of the tumor control rates have been very high, so regardless of whether the LQ model can fit or not, to me it is quite interesting to seek the underlying mechanisms. No matter what we believe, the truth is still the same - some day we will know for sure.

Thanks!

Jimm

No matter what we believe, the truth is still the same.
Seek the truth, and believe it!
Now key people from all sides of the debate are
• writing HyTEC papers together
• presenting in this session together, and
• beginning to understand all sides together…

"We can all win together!!"

A hint from AVM

• In the late 1960s, obliteration of arteriovenous malformation (AVM) demonstrated one of the first clinical successes of single fraction SRS.
• It is commonly observed that a single SRS treatment with only 15 to 25 Gy completely obliterates 80% to 90% of small AVMs, which implies that immature and abnormally formed vasculatures are radiosensitive.
• Special thanks to Raymond Schulz for helping me to realize this — after Faiz Khan’s Suntha lecture at Jefferson, on the way to the train station…
HyTEC Vision Papers: Rationale and Evidence for SBRT

Dr. Victoria Yu, PhD, UCLA
Radiation therapy dose response modeling and optimization of fractionation schedules with cancer stem cells

Dr. Chang Song, PhD, U Minnesota
Role of vascular damage and tumor microenvironment in the response of tumors to SBRT and SRS

Dr. David J. Carlson, PhD, UPenn
Biological dose escalation and outcomes modeling in the era of stereotactic radiotherapy

Dr. Ariel Marciscano, MD, MSKCC
Immunomodulatory Effects of SBRT: Preclinical Insights and Clinical Opportunities

Moderators: Dr. Jimm Grimm, PhD and Dr. Jinyu Xue, PhD