

The Role of Program Project Grants in the Study of 3D Conformal Therapy, Dose Escalation and Motion Management

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LEADING THE QUEST

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Disclosures

- No current conflicts
- Member, Radiation Oncology Health Advisory Council (ROHAC) for the Radiation Oncology Incident Learning System (RO-ILS) supported by ASTRO/AAPM/ClarityPSO
- Previous research and/or travel funding from Varian, Elekta, Scanditronix, Siemens, Sun Nuclear



PPGs in the Study of 3D Conformal Therapy, Dose Escalation + Motion Management

- What is a Program Project Grant?
- PPGs in Radiation Oncology
- Benefits of the PPG Mechanism:
Examples from 3-D, Dose Escalation,
+ Motion Management
- Conclusions



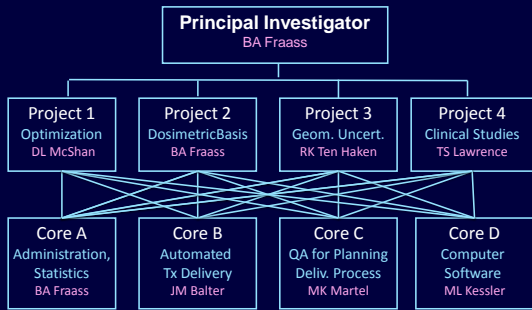
Program Project Grant (PPG)

- A broad-based, multidisciplinary, often long-term research program with a specific major objective or theme addressed by a number of research projects
- A PPG has a central research focus, in contrast to the narrower thrust of traditional research projects
- Each project contributes to the common theme of the PPG, and is usually led by an established investigator
- Provides support for core components which facilitate the projects and overall research effort



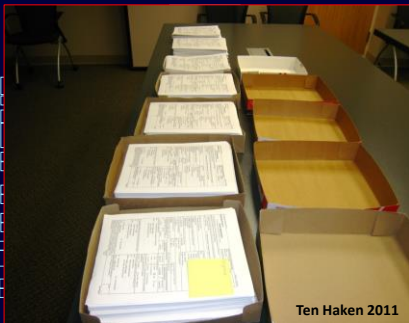
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Optimization of High Dose Conformal Therapy



UM PPG 2000

Program Project Grant (PPG)



Ten Haken 2011

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PPGs in Radiation Oncology

Protons at the Harvard Cyclotron (Suit):

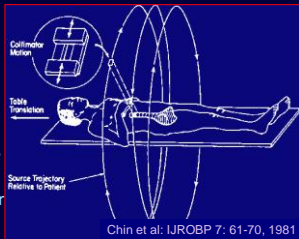
- Proton Tx 1961-2002
- Fiducial-guided setup
- Sophisticated 3-D positioner
- 3-D Eye Plan – Goitein
- More Later...



PPGs in Radiation Oncology

Joint Center for Radiation Therapy (Bjarngard): Computer-Controlled Tx

- First computer-controlled accelerator treatments
- Development of independent jaws, machine control, dynamic wedges
- Treatments that look similar to VMAT, tomotherapy





CN Coleman et al, IJROBP 47: 1357-69, 2000



PPGs in Radiation Oncology

UCSF/Berkeley: Particle Therapy at the Bevalac (Castro):

- Tx with Carbon, Argon, etc
- Image registration
- DVH analysis
- Measuring organ motion
- Imaging dose deposition
- Lots of radiobiology
- ISAH, Isocentric Stereotactic Apparatus for Humans
- Lyman NTCP model

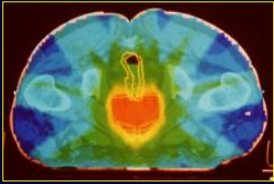



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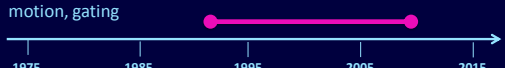
PPGs in Radiation Oncology

MSKCC: Develop New RT Techniques to Improve Local Control (Ling):

- Practical implementation of 3DCRT; MLC; computer-controlled Tx, DMCL IMRT
- Dose escalation: nasopharynx, prostate, lung
- TCP/NTCP + biophysical models, optimization
- Uncertainties + Tx error, DIBH, motion, gating



Mohan et al: Radiother. Oncol. 32, 232-248 (1994)



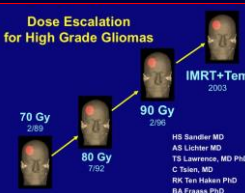
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PPGs in Radiation Oncology

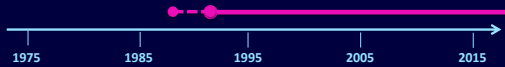
UM: Optimization of High Dose Conformal Therapy (Fraass-TenHaken):

- 3D Planning + Tx, Optimization, SMLC IMRT, Motion, Fncct Imaging
- Dose Escalation: Liver, Lung, Prostate, Brain
- H/N Parotid-Sparing, pharyngeal constrictors, SIB IMRT
- PET, SPECT, MR Fncct. imaging for response-driven adaptation

Dose Escalation for High Grade Gliomas



70 Gy 2/89
 80 Gy 7/92
 90 Gy 2/96
 IMRT+Tem 2003
 HS Sandler MD
 AS Lichter MD
 TS Lawrence, MD PhD
 C Tsien, MD
 BK Ten Haken PhD
 BA Fraass PhD




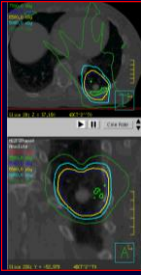
1975 1985 1995 2005 2015

PPGs in Radiation Oncology


VCU-MCV: : Image Guided Adaptive Radiotherapy (Williamson):

- Interfraction motion effects (prostate, cervix)
- 4D RT and tracking, in lung
- Probabilistic treatment planning
- Deformable image registration and dose mapping





Seibers - VCU



PPGs in Radiation Oncology

Some other technically-inclined RT PPGs:

- MD Anderson: radiobiology
- U Wisconsin (Mehta): Tomotherapy
- MGH-MD Anderson: Proton Therapy
- MSKCC: Tumor Hypoxia Imaging (Ling) 2006-2012

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Advantages of the PPG Mechanism

Continuity which allows long-running projects to follow promising leads

70 Gy
2/89

80 Gy
7/92

90 Gy
2/96

Protocol Enabled by:
Many years of diffusion MR, FDG PET, C11 Methionine PET, Image registration, inverse planned IMRT, correction for fractionation, functional imaging analysis tool (FIAT)

Advantages of the PPG Mechanism

Integrated development, testing and use of new techniques which allow more sophisticated clinical studies

MSKCC PPG

3D Planning, NTCP, etc., MLC, IMRT

P1: Dose Esc Lung, Nasopharynx, Prostate to 80Gy

P1: Dose Esc Lung+NTCP, Nasopharynx, Prostate to 86.4 Gy

Lung: Veff vs toxicity, Nasoph SIB 70.2Gy, Prost: 75.6 vs 86.4, 81Gy+9 to MRSI

P2: Biophysical TCP + NTCP Models, simulated annealing

P2: Optimization, non-coplanar, better biol. indices for models

P2: Gating (lung) for IMRT, CT, PET, Image Reg., MV CBCT

P3: MLC Dose Calc, incorp. uncert's, assess outcome influence

P3: DIBH, pelvic setup improvement, eval of setup uncert -> optimizing margins

P3: 3D Imaging, respiration-correlated CBCT, prostate deformation

88, 90, 92, 94, 96, 98, 00, 02, 04, 06

Advantages of the PPG Mechanism

Integrated development, testing and use of new techniques which allow more sophisticated clinical studies

Example:
Liver and lung dose escalation using iso-NTCP-based protocols

Lynen Description, Iso-NTCP Contours

Fractional Volume

Dose (Gy)

1%, 5%, 20%, 50%, 80%, 95%, 99%

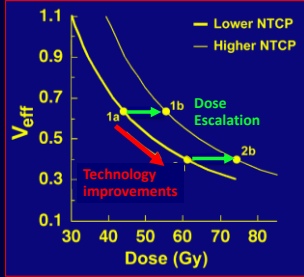
Ten Haken et al: IJROBP 27:68-695, 1993

Advantages of the PPG Mechanism

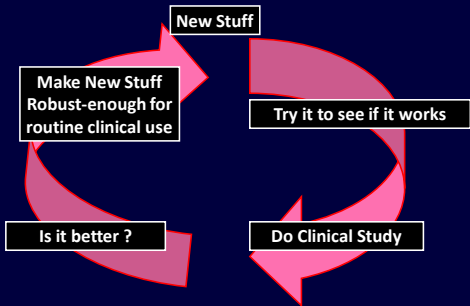
Integrated development, testing and use of new techniques which allow more sophisticated clinical studies

Technical improvements (e.g. motion control, ABC, IMRT, etc) move plan along dose-vol curve, "w/in protocol"

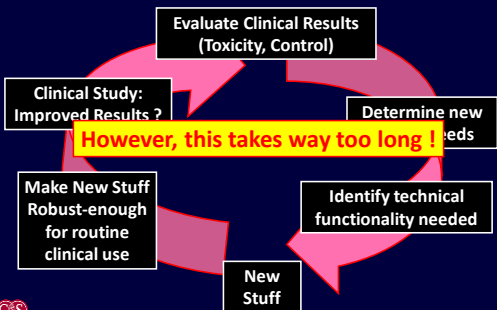
Dose esc. depends on the normal tissue dose-vol-toxicity relationship, not any particular technology, so new techniques are allowed!



Typical Paradigm for New Technology Development?



Typical Paradigm for Clinical Development ?



Advantages of the PPG Mechanism

Integrated clinical and technical development and testing

Within the PPG mechanism, there is enough freedom so:

1. Clinical and technical timelines can run concurrently
2. One can work to predict technological needs many years ahead
3. It is possible to get the clinical data necessary to effectively use the new stuff
4. This freedom allows us to design trials to study clinical changes which are made possible by a new technology, not the technology itself



Stuff

Advantages of the PPG Mechanism

Support for infrastructure and developments necessary for clinical implementation of new ideas + technology

PPG cores provide shared support for the research, and also partial funding for clinical implementation

For example, Cores in the MSKCC PPG included work on:

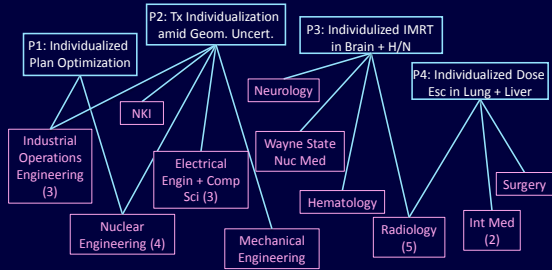
- The SPIN (simulation/portal image network) project
- The dosimetry of dynamic MLC for photons and electrons
- Advanced planning tools for computer-aided optimization



MSKCC PPG 2002-07

Advantages of the PPG Mechanism

Supports broad collaborations and multidisciplinary research efforts

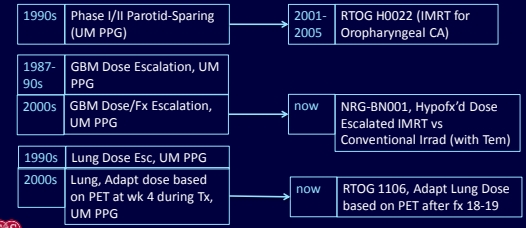


UM PPG 2005

Advantages of the PPG Mechanism

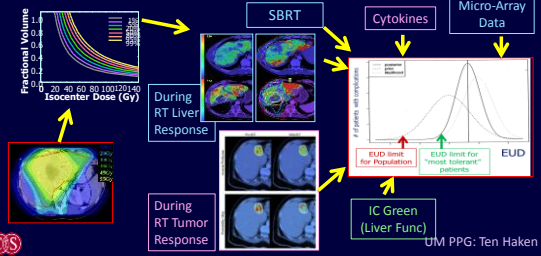
Phase I/II studies performed by PPGs have a harmony, synergy + synchrony that feed big clinical trial mechanisms

The large NRG/RTOG trials that have a significant effect on standard practice are often based on the early phase I/II studies that PPGs often make possible:



Advantages of the PPG Mechanism

Flexibility which allows studies to evolve from technology-enabled trials to advanced response-outcome trials leading to adaptive (precision medicine) trials



Advantages of the PPG Mechanism

The "PPG created the framework for high level intra-departmental collaboration --- it . . . got everyone going in the same direction" -- J Seibers (VCU-MCV)

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Conclusions

- PPGs provide relatively unique and major funding for multi-faceted, interdisciplinary projects which support complex + long-term clinical research
- The coordinated clinical and technical development and testing strategies allowed by the PPG funding have been (at least partly) responsible for a wide variety of clinical advances – in 3-D, IMRT, dose escalation, sophisticated conformal therapy, adaptive therapy, 4-D, motion management, and many other advances that have become the standard of practice in the field



Acknowledgements

| | |
|-----------------|----------------|
| Jim Deye | NCI/NIH |
| Clifton Ling | MSKCC |
| Radhe Mohan | MSKCC, MDAH |
| Jeff Seibers | VCU, UVa |
| Randy Ten Haken | UM |
| Marc Kessler | LBL, UM |
| Michael Goitein | MGH, PSI |