Planning Approaches and Methods for the Treatment of Synchronous Multiple Primary Lung Cancer

Yolanda King BA, BS, RT(T), CMD
Senior Medical Dosimetrist
Anne Arundel Medical Center
Annapolis Maryland

DISCLOSURES
Yolanda C. King, BA., BS. RT(T), CMD

FINANCIAL RELATIONSHIPS:
Employed by Anne Arundel Medical Center
Anne Arundel Medical Center funded the research and my travel

NON FINANCIAL RELATIONSHIPS:
Member of AAMD, ASRT and ARRT
What do you Expect?

- Convince you that using critical thinking and a team approach are key to solving these complex dosimetry issues.
- Share a really cool approach that the team at AAMC took to solve a departmental issue.
- Constantly question and use creative ways to evaluate and analyze dose.
- Challenge you and implement and focus on new methods like this in the future.

Implement the 3 C’s!
Camaraderie-Creativity-Craftsmanship

Geaton & JoAnn DeCesaris Cancer Center

- Located on the Beautiful Chesapeake Bay
- 85 patients a day
- 3 Certified Radiation Oncologist
- 3 Certified Clinical Physicists
- 3 Certified Medical Dosimetrist
- 12 Certified Radiation Therapist
- 3 LINACS 1-2100EX’s (OBI) 1-Novalis TX (Exact Trac) 1-TrueBeam (OSMS/Calypsos)
- Special Procedures: SRS/SRT Cranial, SBRT (Lung, Spine, Pancreas, H&N and Liver) HDR Cylinders+ SAVI and LDR Prostate Seed Implants
- Eclipse Treatment Planning (AAA+ Acuros+ Monte Carlo)
- I-Plan Brain Lab Treatment Planning for SRT
- 4-D CT’s for all SBRT candidates
The Department HUB

Integrate all facets of the department.

Team Development

- SYNERGY IS KEY
- Morning Conference
- Daily team meetings
- Highlight possible issues
- Therapist will push us
- Highlight Achievable results
Grassroots Approaches

- Dive in and develop programs
-Dosimetric role? Creativity!
- Misconception of Independence
- Talk about new technology
- Advantageous because we were able come together to implement strategies and develop programs.

NOVALIS TX MACHINE

Novalis Tx Machine was purchased 2011 with a vision
You Have to Start Somewhere

HOW? Classic traditional developed SBRT protocols
RTOG 0813 (CENTRAL) or RTOG 0236 (PERIPHERAL)

The Journey Began...

WHERE? Anne Arundel Medical Center (AAMC)
WHAT? Lung SBRT Program
WHEN? February 2012
WHO? Inoperable Early Stage NSCLC
WHY? Co-morbidities/Low Pulmonary Function Test (PFT's)
SETTING BOUNDARIES

- Accurate positioning of the tumor is key!
- Decrease Normal Tissue Complications
- Increase Tumor Control Probability
- Positioning can be difficult in the Pulmonary region due to intra-fraction motion. (3-5cm)

Bronchial Tree+2cm is Boss

“High Risk Treatments”

- Early toxicity is often seen
- Determines the fraction size
- Can be very fatal
- Proceed with caution when lesions abut this structure
Playing by the Rules

RTOG 0813 (2009)
- Centrally located tumors
- Total doses 50Gy (10Gy per Fx)
- At least 24 hours between Fx’s
- Normally 10 beams no less than 7 beams (non-coplanar)
- Energies no higher than 15Gy can be utilized
- Minimum field size 3.5cm

RTOG 0236 (2002)
- Peripherally located tumors
- Total doses 54Gy (18Gy per Fx)
- At least 40 hours between Fx’s
- Normally 10 beams no less than 7 beams (non-coplanar)
- Energies no higher than 15Gy can be utilized
- Minimum field size 3.5cm

Conformality is King

RTOG 0813 (Central)
RTOG 0236 (Peripheral)

Conformality at a Distance is being Analyzed!

INCREASE TCP  DECREASE NTC
WHAT ABOUT THE OAR’S?

RTOG 0813 (Central) 2009

RTOG 0236 (Peripheral) 2002

Dose Analyzation with cc’s was adopted!

Max Point Dose Analyzation

Rules are Made to be Broken!

- RTOG 0236 started in 2002 Ended in 2016
- RTOG 0813 started in 2009 Still Active
- Our Patients weren’t truly under protocol
- What are ways we can approach treating our patients that would be beneficial to our department

Rules are Made to be Broken!
Noticeable Trend

- Begin to notice that some patient were becoming “frequent flyers”
- OAR Sparing in these cases truly became an issue
- Different fractionation
- Co-morbidities
- Quality of life can come at a cost

Think Outside the Box

- How do we keep conformality and TCP while minimizing some of the technical constraints found within the protocols?
- What were some of the pit falls we were experiencing departmentally?
  - Too many couch kicks (CONFORMALITY/NTC)
  - Multiple CBCT’s lead to excessive time on the table (MOTION)
  - Do you need 10 beams? (GEOMETRY OF BEAMS/NTC)
  - Why not arcing techniques? (TIME : POSITIONING)
  - Toyiing with fractionation (NTC)
  - Adjusting beam weights (GEOMETRY OF THE BEAMS)
Who wins the Battle?

- Patient specific OAR goals
- Therapist? Time on the table/patient discomfort
- Physician? Conformality/NTC/Morbidity
- Physics? Cumulative dose effects/Deliverability/TCP
- Dosimetrist will always win (3C's)
  - Chance to push the culture
  - Strengthen the team
  - Learn new ideas
  - Advances entire field

What Causes the Oglio Trend?

- These patients used to be qualified as palliative
- Better staging development for these subgroups of patients
  - “Stage migration” 4 → 3
- Better imaging (PET, CT, MR)
- In-transit met vs Hematogeneous.
  - In-transit derives from skin to lymphatics
  - Hematogeneous derives from tumors with drainage directly into the lung
Evaluate the Perception/Reality

- 14 patients presented with Oglio Mets to the lung within a 9 month span.
- Is this our new normal?
- Patients were receiving treatment to both sites sequentially
  - RE-CT as a new patient
  - Patients were taking up time on the table
  - Patients personal time and commitment was beginning to be a patient dis-satisfier
- Financial commitment to the patients

Time to Re-Evaluate our Approach

- How can we develop a method to increase patient satisfaction
- Decrease time on the table
- While targeting the Oglio Mets considering TCP and NTC
- SYNCRONOUS DELIVERY!
Meeting of the Minds

**PRO’s**
- Time on the table
- Patient payment responsibility
- Shortened courses of Therapy
- Use of Arc Therapy
- Freedom of creativity
- Effective doses to the necrotic core
- Fewer Appointments for Patients Travel Long Distances

**CON’s**
- Uncertainty about dose no data
- No clear cut approach to follow
- Takes time to build a program
- How do you assess the OAR limitations and coverage
- Dosing schemes

AAMC’s Planning Paradigm Shift

- Synchronous delivery
- Dose Modulation
- Run different fractionation schemes
- Cater to patient specific needs
- Possible wins for the patient/department
- No data is never good in Radiation Oncology.
- What are the possible side effects to the patients
New “Protocols” In Town

- RTOG 1021 Gave Dose Limits to additional structures at 54Gy range.
  - Ribs
  - Brachial Plexus
- August 2012
- Limited patients/Terminated

- Joint Lung Cancer Trialist’s Coalition (Stablemates) also gave dose limits in the 54Gy range.
  - Rapid Arc Introduction
- April 2015
- AAMC is currently enrolled with patients slated to be on protocol

Inaugural Synchronous Attempt

83 y.o. Female with a history of smoking presented with malignant neoplasm of the L Lower Lobe/L Bronchus and R Upper Lobe/ R Bronchus
Planning Parameters

6FFF 4 NON COPLANAR ARCS
C/I L=0.98     C/I R=1.01

Inaugural Synchronous Attempt
Cont’d.

RUL not touching the Bronchial tree+2 so peripheral fx possible
LLL was inclusive of the Bronchial tree+2 so central fx possible

* When both are being delivered simultaneously how do you critique the normal tissue?
* What takes precedence?
The Verdict

RUL Peripheral Legion 54Gy/3 Fractions (SBRT Treatment)
LLL Central Legion 60Gy /8Fractions (Hypofractionated Treatment)

Takeaways

• This issue is considered a Gray Zone for many Radiation Oncologists.
• Can local control be achieved.
  • Primary function of Rad tx.
  • Should chemo be considered?
  • If Rads first chemo gets complicated
  • If SBRT is considered first the recommendation is Hypofraction 60Gy in 8fx
    • Golden Number in SBRT 100BED
    • This Fractionation yields 105BED (10A/B)

Vol.99, No.4, pp. 766-768, 2017
It was determined by the Physics group that we need to establish stronger parameters that would help move the physicians forward.

- Maybe the inaugural case was not the best because the lesions were on opposite sides. Could lead to peripheral toxicities.
- Lung isn’t a pelvis!
  - Parallel structure/ Serial structure constraints
  - Geometry and Conformality for NTC
  - DO NO HARM! And ALARA principles to consider

Very uncomfortable with traditional doses

- Whitmore’s Principle “Is cure possible only when it is necessary, or in this context “is control possible only?”
  - CURE VS CONTROL
  - Widespread metastatic disease is typically amenable to localized therapy.
  - ARE YOU TRULY BUYING THE PATIENT TIME? Less Complication/Morbidity
  - Chemo can be delivered

More comfortable combined dose schemes

- Presents problems with Synchronous delivery
- WHAT ABOUT THE LOW DOSE???
- More conservative dose per fx.
Round Two!

- 76y.o Male Presented with History of smoking, COPD, O2 Dependency
- Malignant Neoplasm of the Anterior and Posterior R Lung

Round Two cont’d.

- Measurements may present a huge issue
- Smaller targets allow for faster dose fall off than medium or larger targets
- OAR doses are determined on dose fall off
- Ant and Post lesion both are categorized as Centrally located 50Gy/5fx is possible.
- What would be the possible setbacks?
The Verdict

Traditional 7Fld 6x Plan Non-Coplanar
R Post Lesion Central
SBRT 50Gy/5 Fractions

Traditional 7Fld 6x Plan Non- Coplanar
R Ant Lesion Central
Hypofractionation 60Gy/8 Fractions

These are Irish Twins

• Cumulative dose numbers are a little nerve racking
• Same Plane
• Try to get as much separation between the doses as possible
• C/I is Paramount!
• R Post C/I= 1.13
• R Ant C/I= 1.12
**Third Time’s a Charm**

- 51 y.o Male, Non smoker presents with Malignant neoplasm of overlapping sites of the right bronchus and lung. Known hypertension, therefore he isn’t a candidate for surgery.

**Size Matters**

- Patient is late stage and technically Stage Migration.
- One lesion is Central and the other is Peripheral
- Comfort and quick delivery was key
- This is a large size PTV
- Dose fall off could be an issue
- Possible increase to OAR’s
How About Conventional?

6FLD N CO-P 6XFFF 151.79cc's C/I=1.13
6FLD CO-P 6XFFF 18.28cc's C/I=1.23

How About the Cumulative Dose

- When reviewing the lesions cumulatively there is a large amount of high dose.
- No space between the RX lines
- Legion size and position causes this phenomenon.
SYNCHRONOUS IS THE WAY

- Total Plan Max Point 72.98Gy
- Sequential Max Point was in the 90’s
- Separation of the Rx dose
- OAR review was extrapolated from RTOG0813 since the dosing and lesion position is similar to central.

Initial Follow-Up

- Patient presented with sore mouth, loss of appetite and fatigue
- Cisplatin and Taxotere were giving concurrently to the Rad
- Was the complications chemo or rad related? (Review doses)
Hypofractionation has a Cost

\[ \text{BED} = n \cdot d \left(1 + \frac{d}{\alpha / \beta}\right) \]

- \(n\) = number of fractions
- \(d\) = fractional dose
- \(\alpha/\beta\) = properties of the tissue we are considering.
  (10 = Early responding
  3 = Late responding)

With the changes in fractionation schemes in SBRT, how do we consider if the treatment is adequate or if the normal tissues are not going to be damaged

- e.g. of early = skin, bone marrow, testes
- e.g. of late = bladder, cord, kidney

BED calcs are performed for ALL Hypo cases.

What dose did the Esophagus Receive?

RTOG 0813 Esophagus

RTOG <5cc’s 27.5Gy (10Gy/FX)
INTERPOLATION <5cc’s 37.1Gy (7.5Gy/FX)
AAMC <5cc’s 31.58Gy

RTOG MAX 5% = 52.5Gy
INTERPOLATION = 64.3Gy
AAMC = 48.34Gy
Ah-Ha Moment!

- Concurrent chemo is often given to patients with NSCLC.
- Yet chemo isn't recommended to patients Stage1 NSCLC.
- Gray area because of staging and not receiving SBRT.
- We are guessing that Chemo was the culprit.
- Possible side effects for Cisplatin and Taxotere include:
  - Sore mouth
  - Taste changes
  - Loss of appetite
  - Feeling of tired

Abscopal Effect

- Tumor response outside of the target region.
- Oligo mets in low dose regions of SBRT lung patients have been observed to be eradicated.
- Is this effect a response from the patients' immune system or is communication between tumor regions?
- Recent studies have noted an increase in the number of cases that witnessed the Abscopal effect.
- The increase could be associated with the improved imaging techniques or is there a mechanism associated with SBRT treatments.
- SBRT and Hypo fractionated treatments may show an increase in abscopal effects in patients.
VICTORY!

- This procedure does provide advantages
- Treated several patients with Oglio (Lung)
- One was delivered synchronous
- Physician Buy In/ Definite usage in the future
- Program development and Understanding
- Maximized 3C’s
- Ultimately each patient is different. Consider all possible limitations.
- What about Hyper Arc limited crossover areas in the future?
  - Cranial only
  - Would be awesome for synchronous

What’s Next for AAMC?
Single Iso Multiple Mets

- Novalis TX Machine
- EXACT TRAC
- MME Algorithm (Multiple Mets)
- Using the synchronous methods with our brain cases.
- Optimizing Is done with Pencil Beam (brain homogeneous)
- Dynamic conformal arcs to treat up to 15 lesions per delivery

Taking Things a Step Further

- Beam's Eye View of one of the dynamic conformal arcs of the treatment plan.
- MLC apertures are in teal.
- Note large collimated opening with a significant portion of the field blocked by MLCs.
- Reduction in treatment time and patient visits
- Patient satisfier
Conclusion

- AAMC has proven that this is an adequate treatment approach for Oglio NSCLC patients.
- Prior to implementing this as a strategy make sure that you consider all patient aspects.
- Synchronous may not be the solution for all patients, but hopefully this will challenge you to implement new ideas.
- Make sure you implement the 3C’s
  - Comradery
  - Creativity
  - Craftsmanship
- Future technologies will push you to consider synchronous treatments.

Thank Yous!!

- Dr.’s Luqman Dad, Angel Torano, and Mary Young
- Anne Arundel Medical Center Dosimetry Staff
  - Evelyn Lagana-McLucas, CMD
  - Ahssan Balawi, CMD
- Brian Hasson, PhD.,
  - Chief of Clinical Physics
- Charles Geraghty, M.S.
  - Clinical Physicist
1. Dose tolerance for Stereotactic Radiological Body Radiation Therapy
2. Lung Metastasis
   https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4448537/
3. RTOG 0813 Protocol
   https://www.rtog.org/ClinicalTrials/ProtocolTable/StudyDetails.aspx?study=0813&mode=broadcasts&ptid=387
4. Docetaxel (Taxotere®) and cisplatin chemotherapy
5. Stereotactic Body Radiotherapy (SBRT) For Lung Cancer Report of the ASTRO Emerging Technology Committee (ETC)
   https://www.astro.org/uploadedFiles/Main_Site/Clinical_Practice/Best_Practices/LungSBRT.pdf
6. ASTRO issues guideline for use of stereotactic radiation in early-stage lung cancer
7. Stereotactic ablative radiotherapy (SABR) in operable early stage non-small cell lung cancer (NSCLC) patients: challenge to claim being undisputed gold standard
   https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4499653/
8. Stereotactic body radiotherapy (SBRT) in lung oligometastatic patients: role of local treatments
9. Radiation therapy and the abscopal effect: a concept comes of age
   https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4828732/
10. RTOG 0236 Protocol
    https://www.rtog.org/ClinicalTrials/ProtocolTable/StudyDetails...