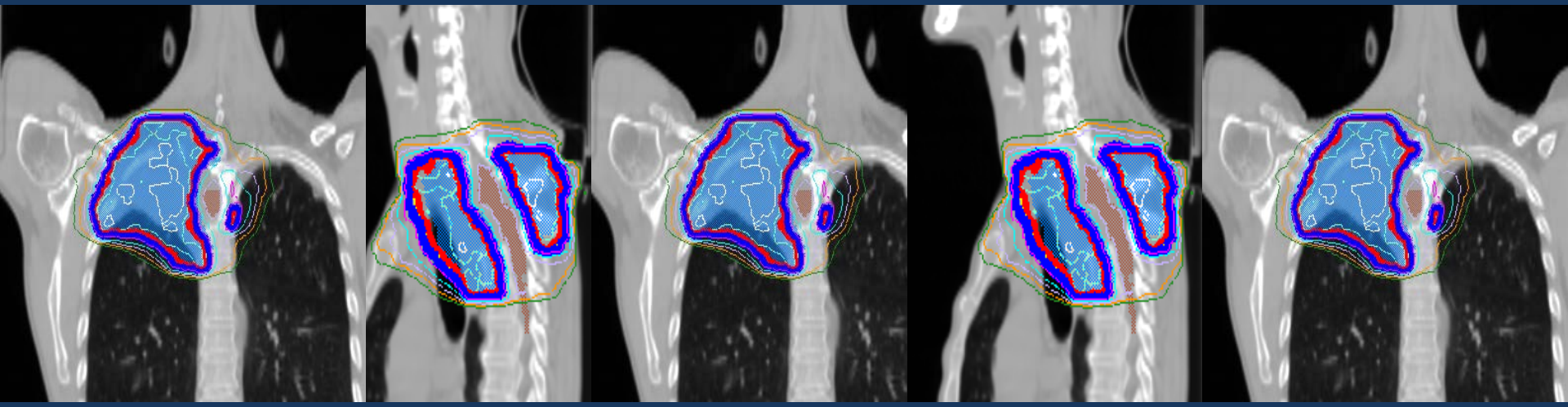
Radiation Therapy for Lung Cancer



Megan E. Daly MD
Associate Professor
Department of Radiation Oncology
UC Davis Comprehensive Cancer Center

Disclosures

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Overview: Current use of radiation for Lung Cancer

- Current Status of SBRT for early stage NSCLC
  - Role in operable patients
  - Next directions
- Current Status of Radiation for Locally Advanced NSCLC
  - Next directions
- Lung cancer palliation with radiation
- Management of radiation-induced lung toxicity

Radiation for Lung Cancer

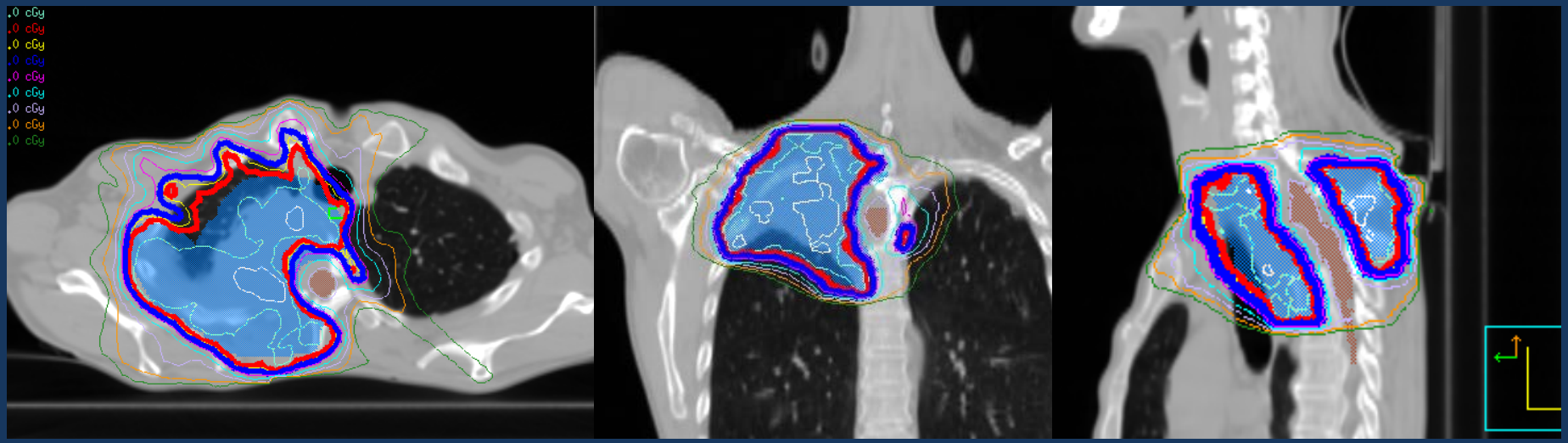
- Early stage medically inoperable disease
- Early stage medically operable (investigational)
- Locally advanced (IIIA/IIIB)
- Small Cell Lung Cancer
- Palliation of metastatic disease
- Ablative therapy for oligometastatic/oligoprogressive disease

Radiotherapy for Lung Cancer: Key Issues

- Minimizing Toxicity
  - Small margins (daily setup is crucial)
  - Accounting for lung motion in the planning process
  - Ability to sculpt dose around critical structures
- Maximizing Tumor Control
  - Ability to deliver ablative doses while sparing normal tissues

Treatment Planning Challenges

- Proximity to critical structures
- Irregularly shaped target volumes
- Moving tumors



Lung SBRT: Overview and Uses

- Use of highly conformal radiation using ablative doses over 1-5 treatments

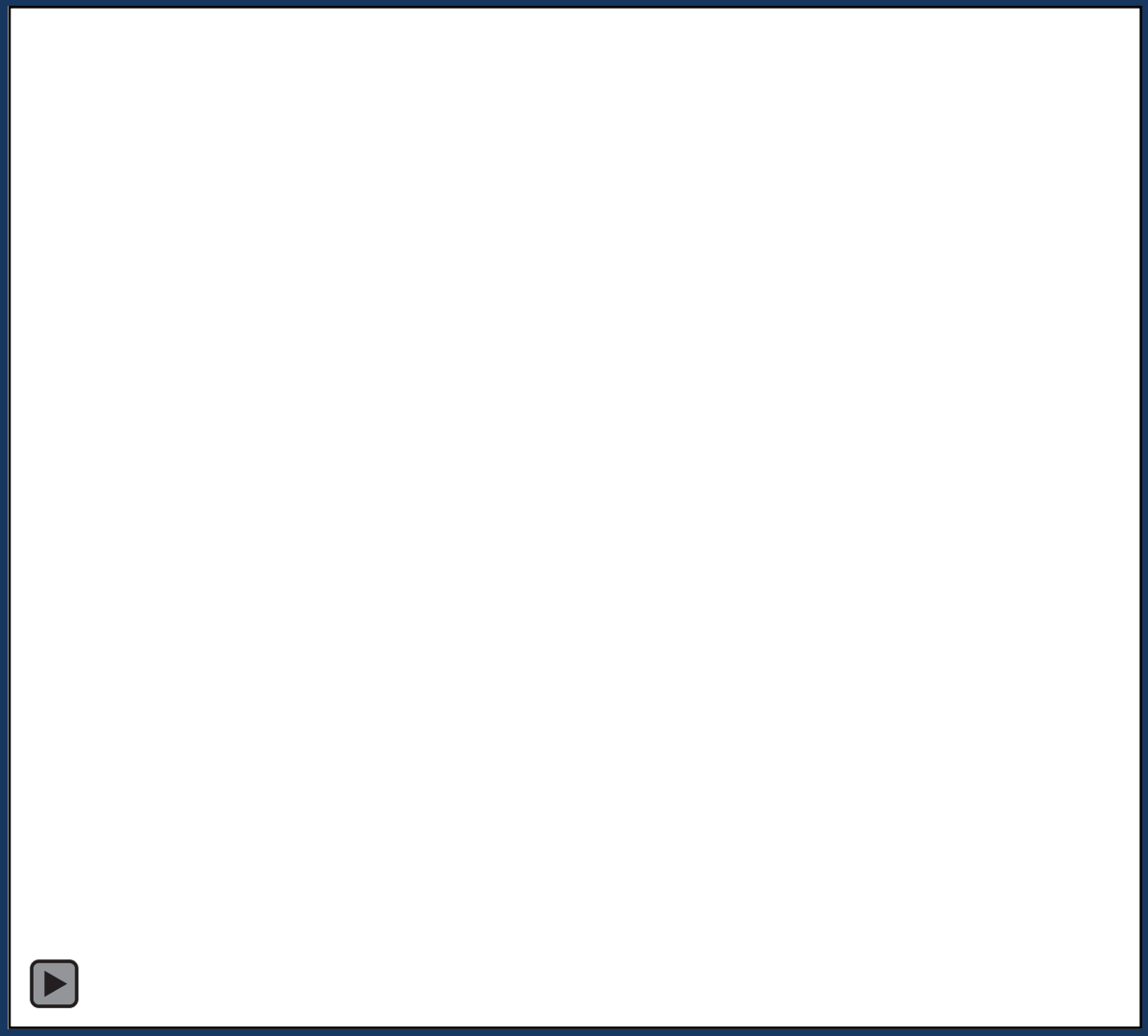
Lung Stereotactic Body Radiotherapy (SBRT)

- Standard of care option for medically inoperable patients with early stage non-small cell lung cancer (NSCLC)
- Non-invasive, outpatient procedure over 3-5 sessions
- High local control rates (>90%)

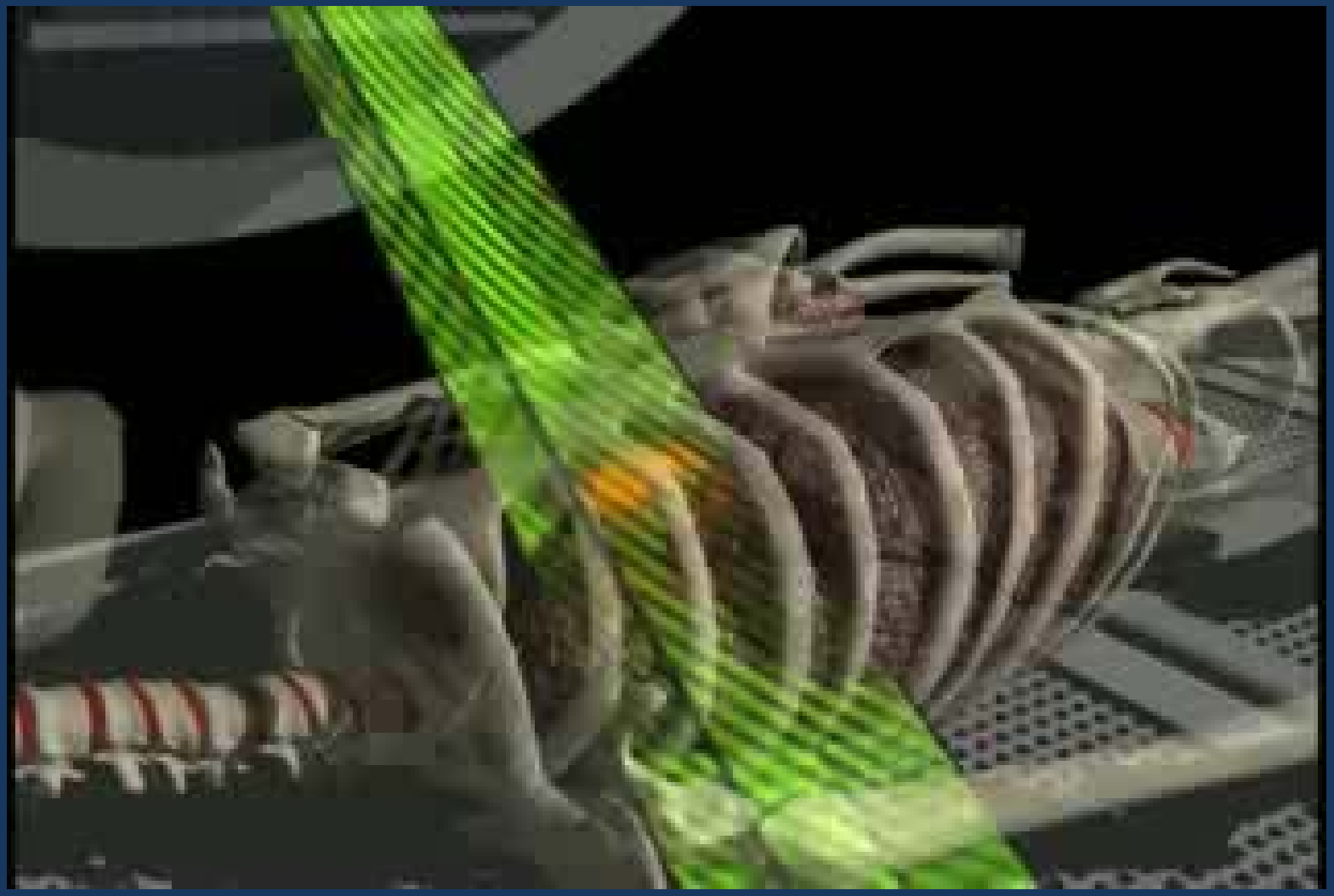
Methods of compensating for respiratory motion

- Free Breathing ITV
- Abdominal Compression
- Respiratory Gating
- Tumor Tracking

Defining an ITV: 4DCT



Respiratory Gating



Abdominal Compression

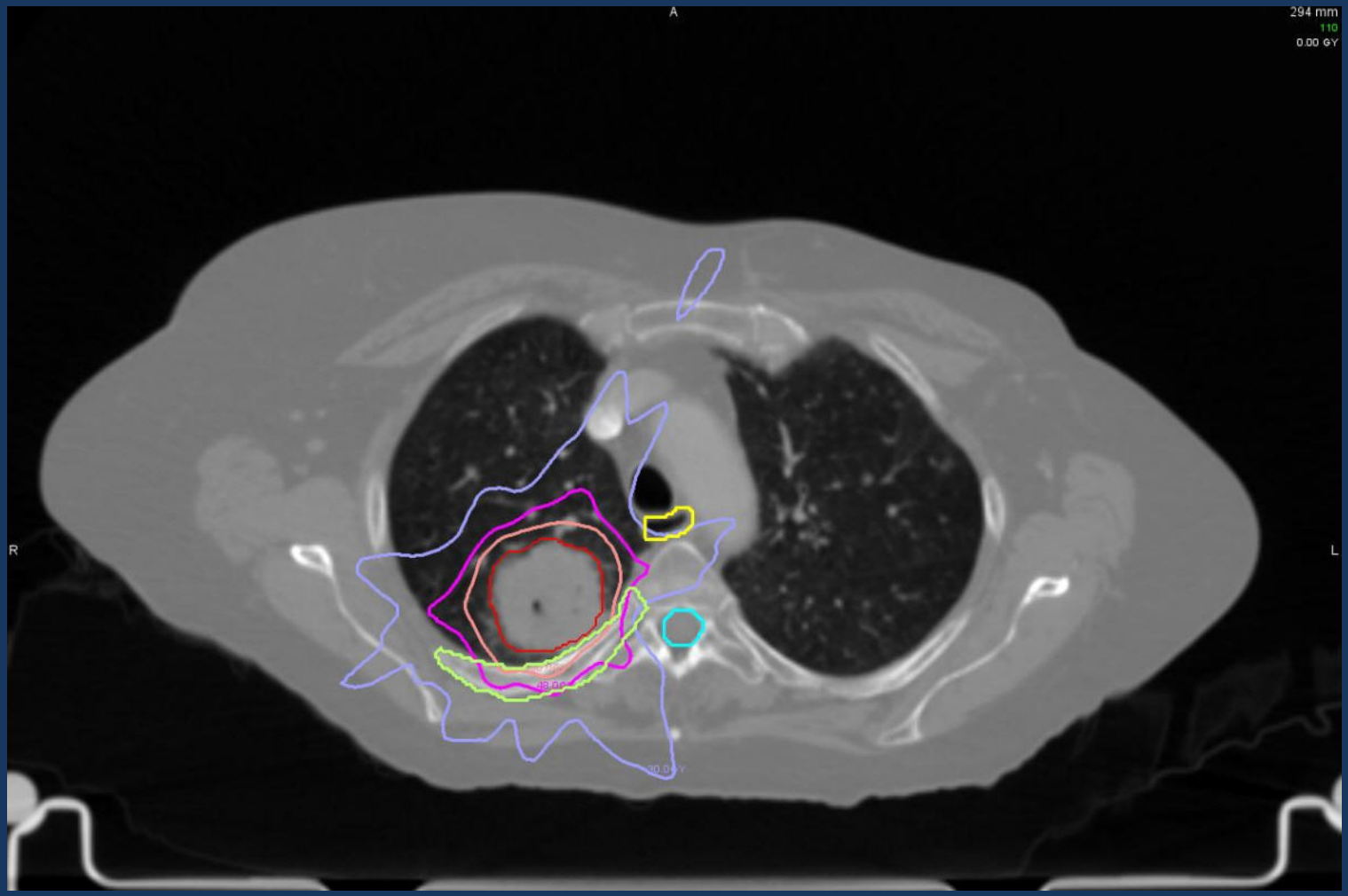
Lung SBRT: Clinical Outcomes
RTOG 0236 (JAMA 2010)

- Phase II study; medically inoperable pts with T1-2 N0 NSCLC
- 54 Gy/3 fx
- 3 yr Primary tumor control 97.6%
- 3 yr Local Control 90.6%
- 3 year Distant Failure Rate:
  - T1: 14.7%
  - T2: 47%
- 3 yr Disease-Free Survival 48.3%
- 3 yr Overall Survival 55.8%
- 3.6% rate of grade 4 adverse events

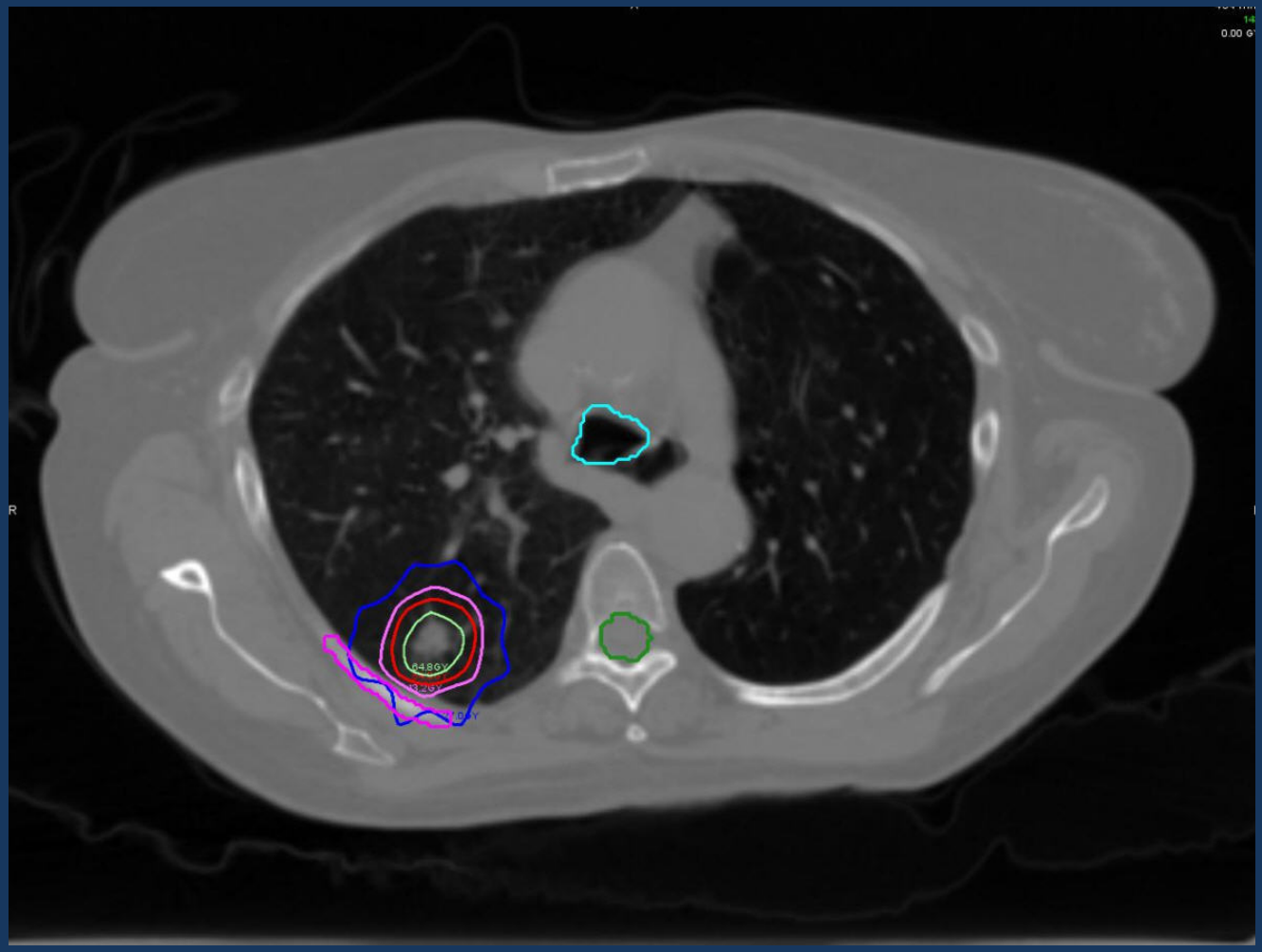
Current Use of SBRT

- Standard Option for Medically Inoperable, peripheral early stage (T1-2 NSCLC < 5 cm)
  - 54 Gy in 3 fractions
- Investigational in medically operable patients
- Investigational for tumors >5cm
- Some concerns of increased toxicity for central lung tumors (within 2 cm of proximal bronchial tree), but protracted regimens of 4-8 fractions are generally considered safe
  - 48-50 Gy in 5 fractions
  - 50-60 Gy in 5 fractions
  - 60 Gy in 8 fractions

Sample SBRT Plan: T2aN0M0 Central NSCLC



Sample SBRT Plan: T1N0M0 Peripheral



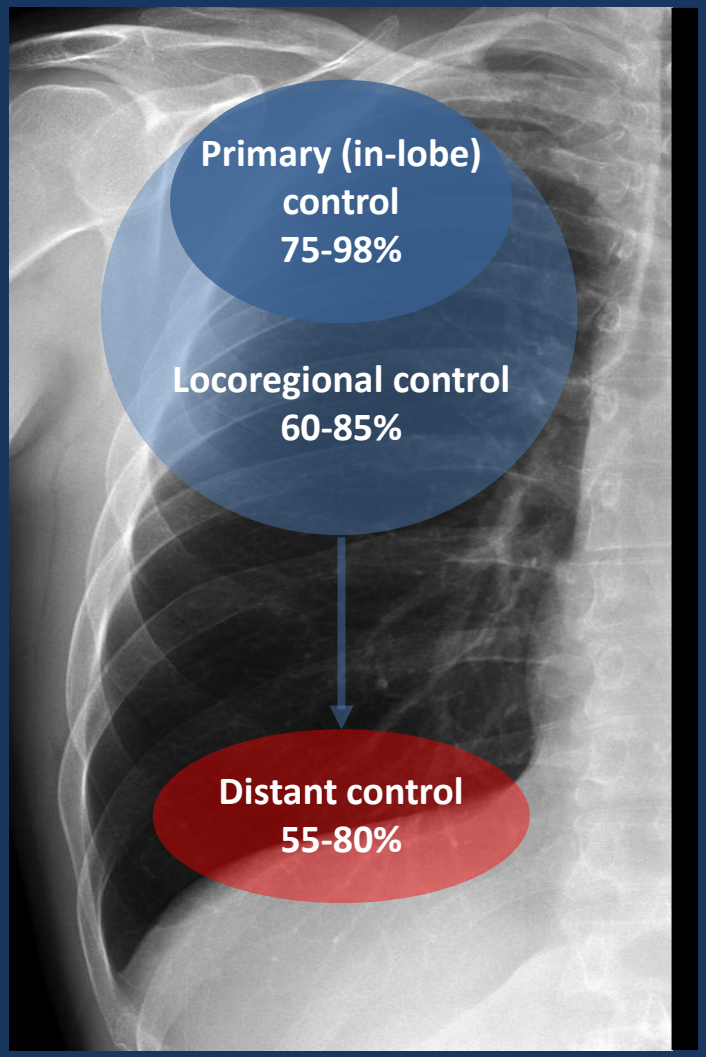
SBRT for Operable Patients: Current Status

- Several studies have attempted to compare surgery and SBRT in a prospective, randomized fashion and failed to accrue
- Many retrospective analyses on this topic, but selection bias remains a major problem
  - Propensity matching attempts to limit the bias of retrospective studies by matching patients on baseline characteristics, and reduces influence of varying baseline characteristics
- Surgical management remains the standard therapy for medically operable patients in absence of completed, randomized trials

Prospective Randomized Trials Evaluating SBRT for Operable Patients

Trial	Eligibility	Design	Status
STARS	T1-2aN0M0 <4 cm, fit for lobectomy	Randomized Phase III comparing lobectomy to SBRT	Terminated due to poor accrual
ROSEL	T1-2aN0M0 <4 cm fit to tolerable lobectomy	Randomized Phase III comparing lobectomy to SBRT	Terminated due to poor accrual
ACOSOG Z0499	Peripheral NSCLC ≤ 3 cm; "high" surgical risk	Randomized Phase III comparing sublobar resection to SBRT	Terminated due to poor accrual
JoLT-Ca STABLE-MATES	Peripheral NSCLC ≤ 4 cm; "high" surgical risk	Pre-randomization design; phase III	Actively accruing
Veterans **A**ffairs **L**ung Cancer Surgery **O**r Stereotactic **R**adiotherapy Trial (**VALOR**)	T1-2N0M0<5 cm fit for lobectomy	Randomized Phase III	Actively accruing
RTOG Foundation 3502 (POSTILV)	T1N0M0 ≤ 3 cm fit for lobectomy	Randomized Phase II	Actively accruing

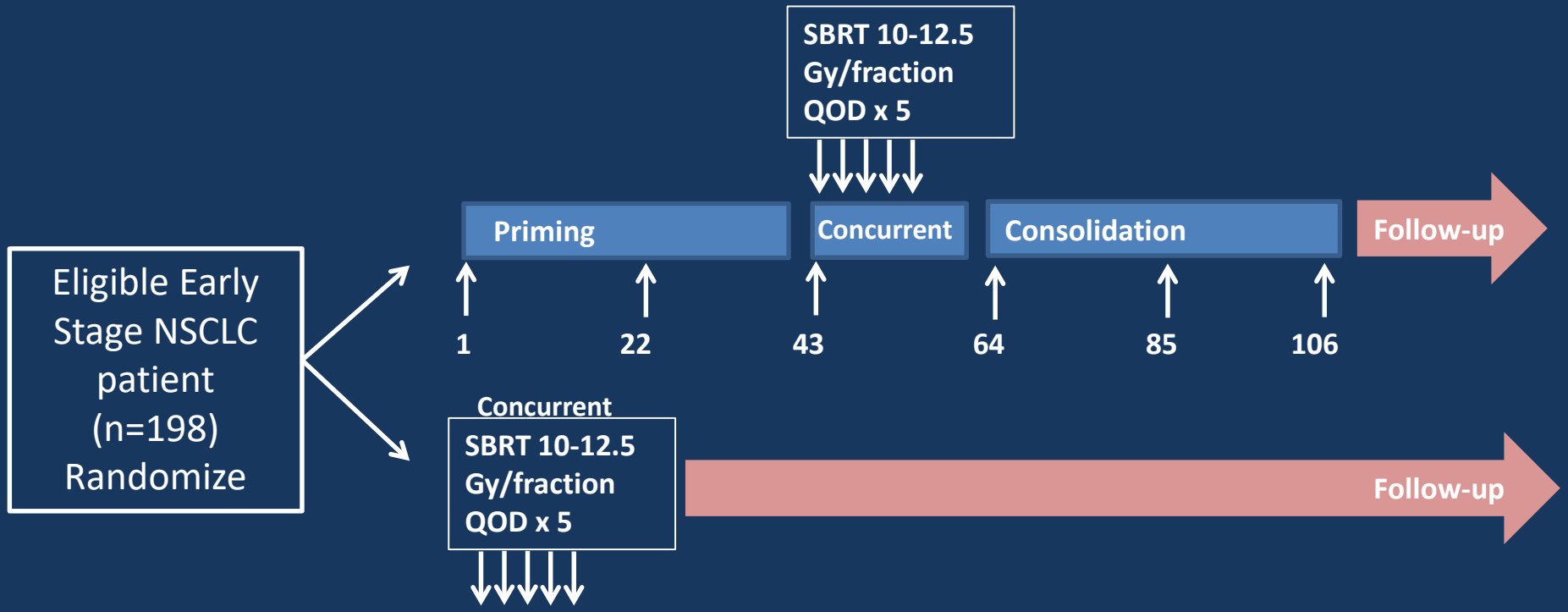
SBRT Patterns of Failure



Next Directions in SBRT

- Strategies to reduce regional/distant failure
  - Adjuvant chemotherapy
  - Immunotherapy
  - Targeted therapy

UC Davis Stage I Trial



(Chemo)Radiation for Locally Advanced NSCLC

- Definitive Concurrent Chemoradiation for Unresectable IIIA/IIIB disease

- Pre-operative CRT for well-selected, resectable IIIA disease with low-burden N2 disease

Defining Targets

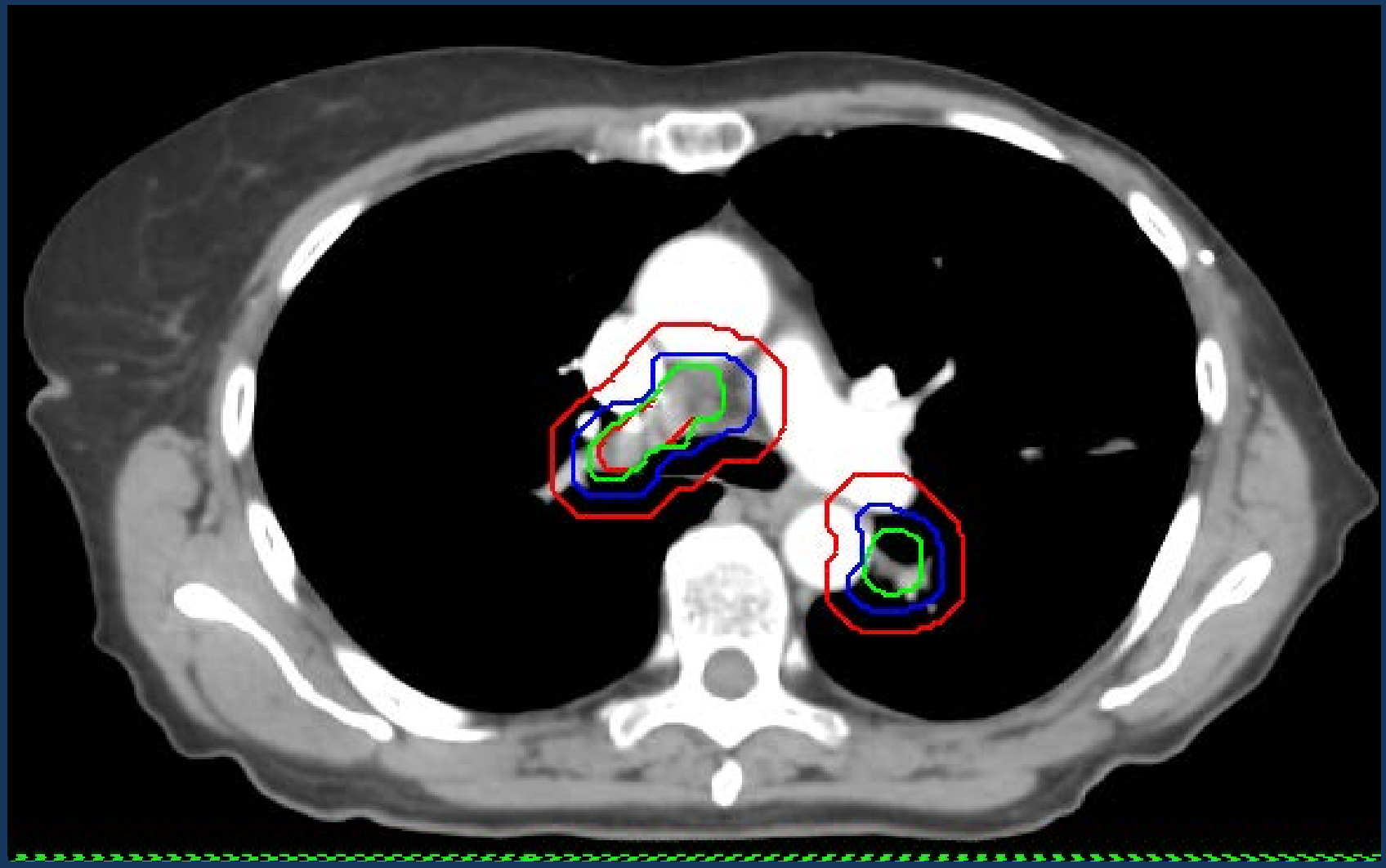
- **G**ross **T**umor **V**olume (GTV): Radiographically involved tumor or nodes
- **I**nternal **T**arget **V**olume (ITV): Encompasses tumor excursion due to respiratory motion
- **C**linical **T**arget **V**olume (CTV): Includes additional margin for microscopic spread
- **P**lanning **T**arget **V**olume (PTV): Additional margin for daily setup error

Locally Advanced NSLC – Technical Advances in RT Planning

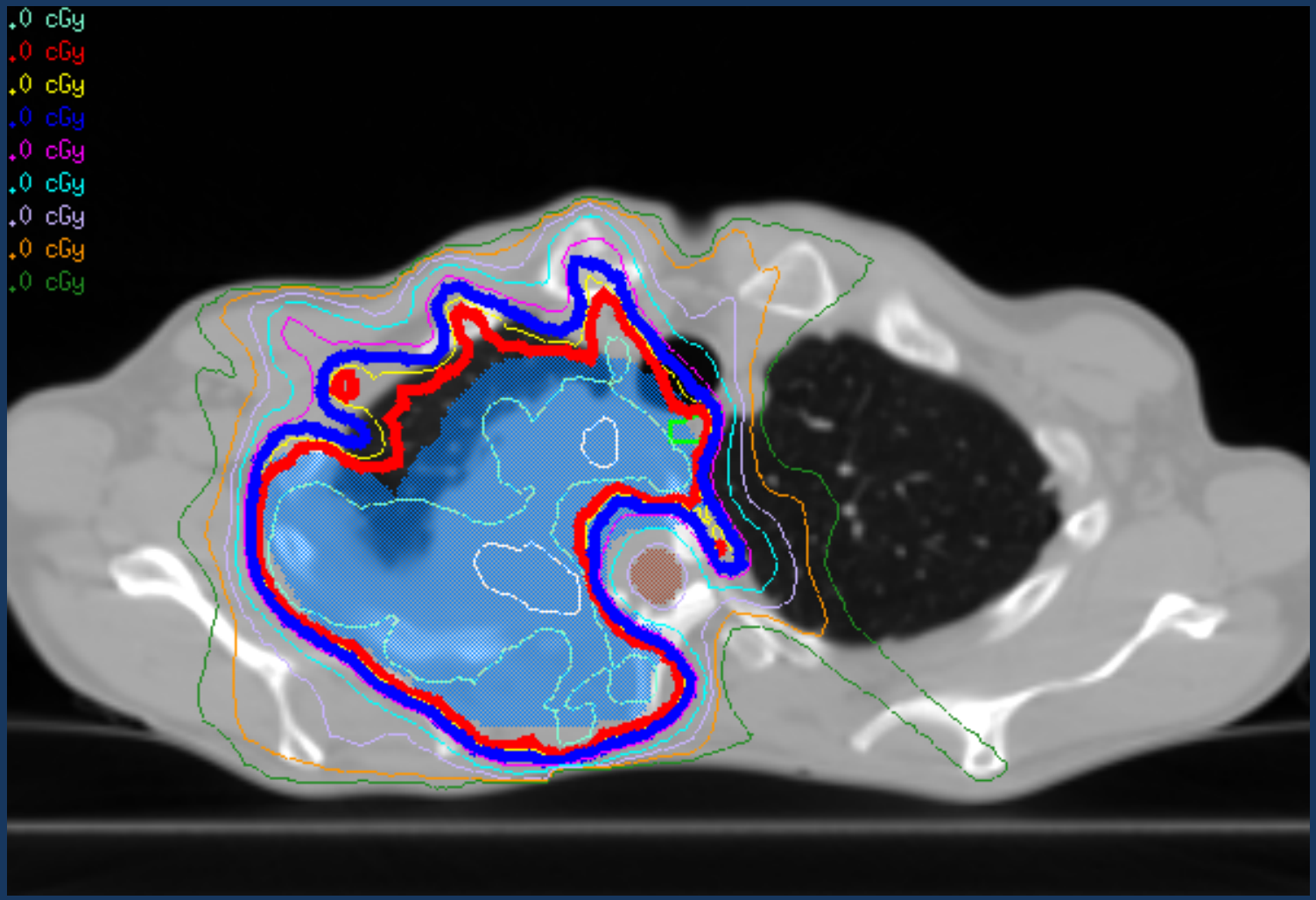
- Intensity Modulated Radiotherapy (IMRT) and Volume Modulated Arc Therapy (VMAT)
  - Allow for concave and convex dose distributions
  - For appropriately selected patients improves sparing of normal tissues
  - Creates sharp dose gradients

- 4D CT simulation
  - Allows accurate estimation of tumor motion with breathing

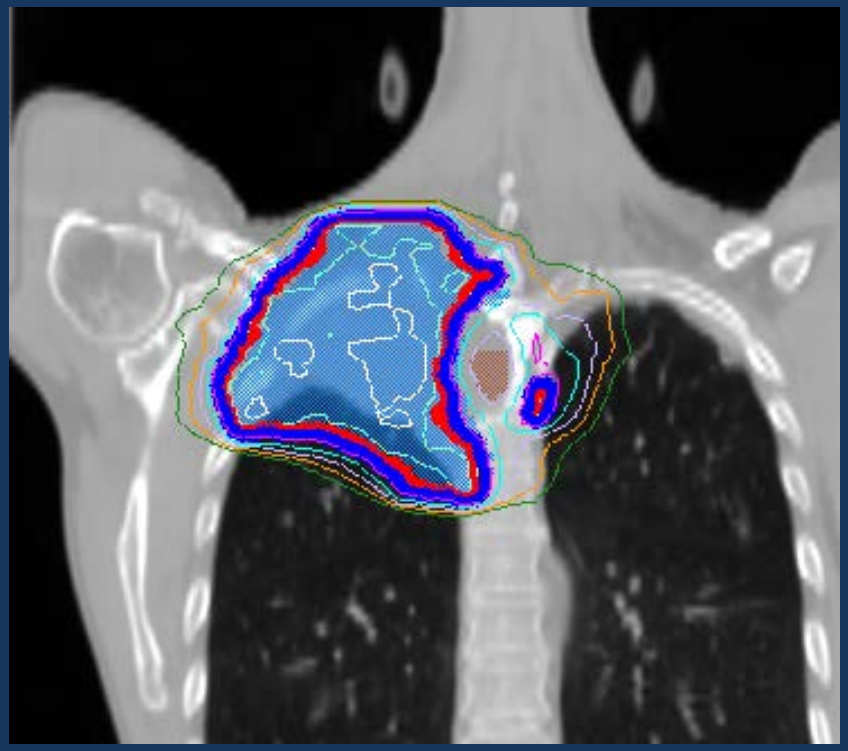
Lung Cancer Target Definition

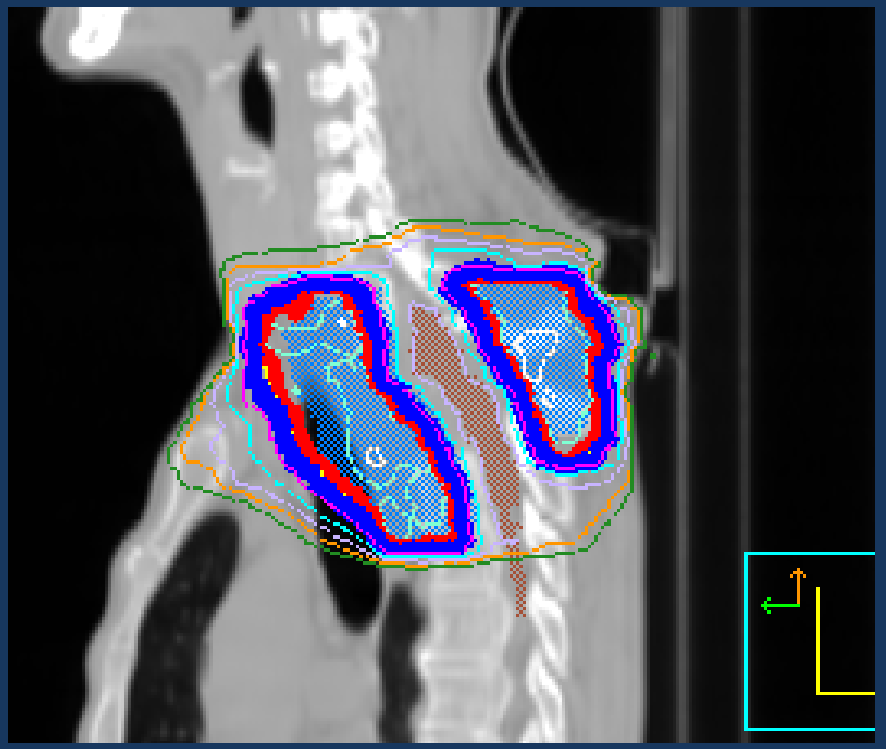


IMRT T4N0M0 NSCLC

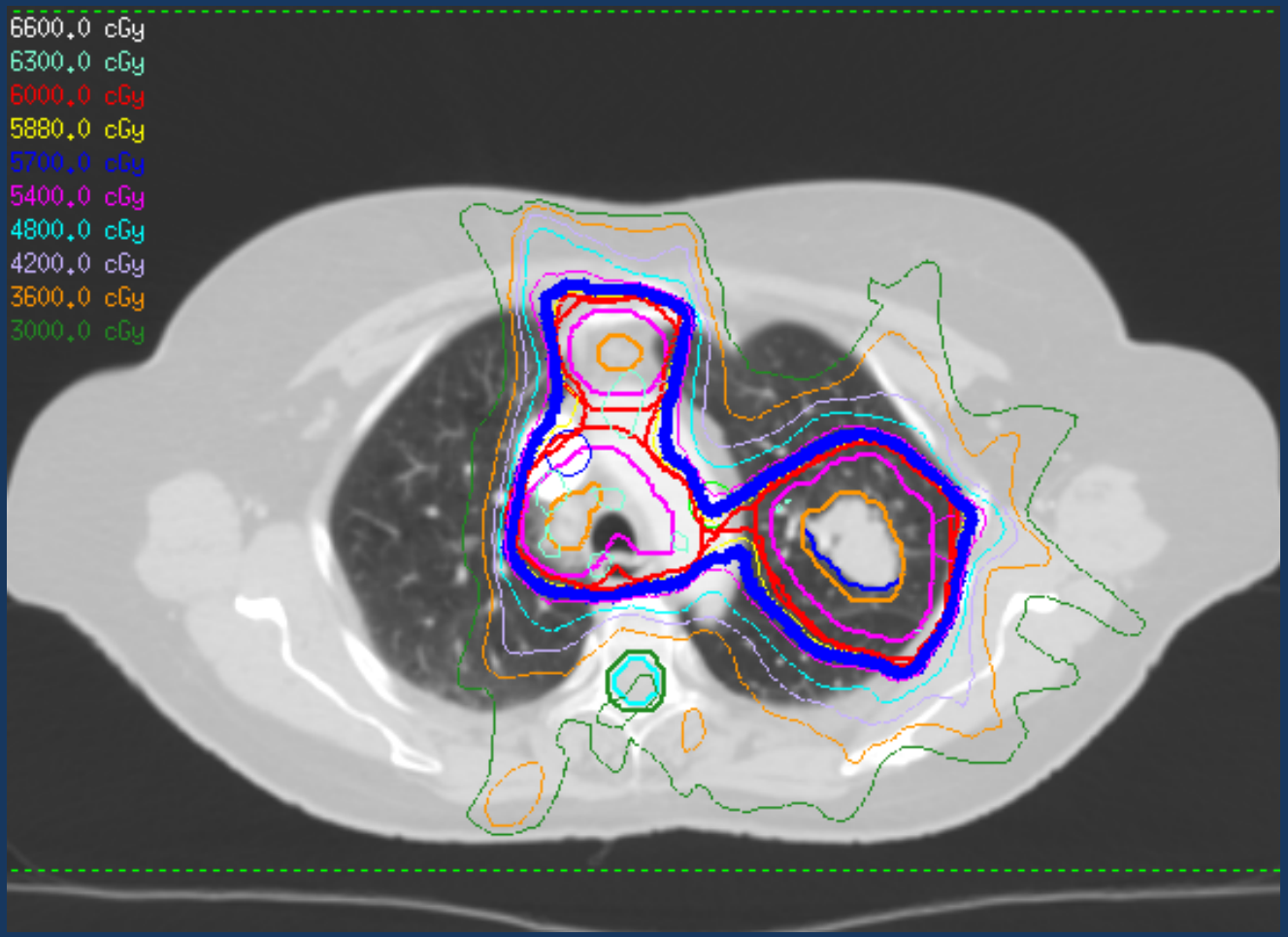


IMRT T4N0M0 NSCLC: Sagittal/Coronal

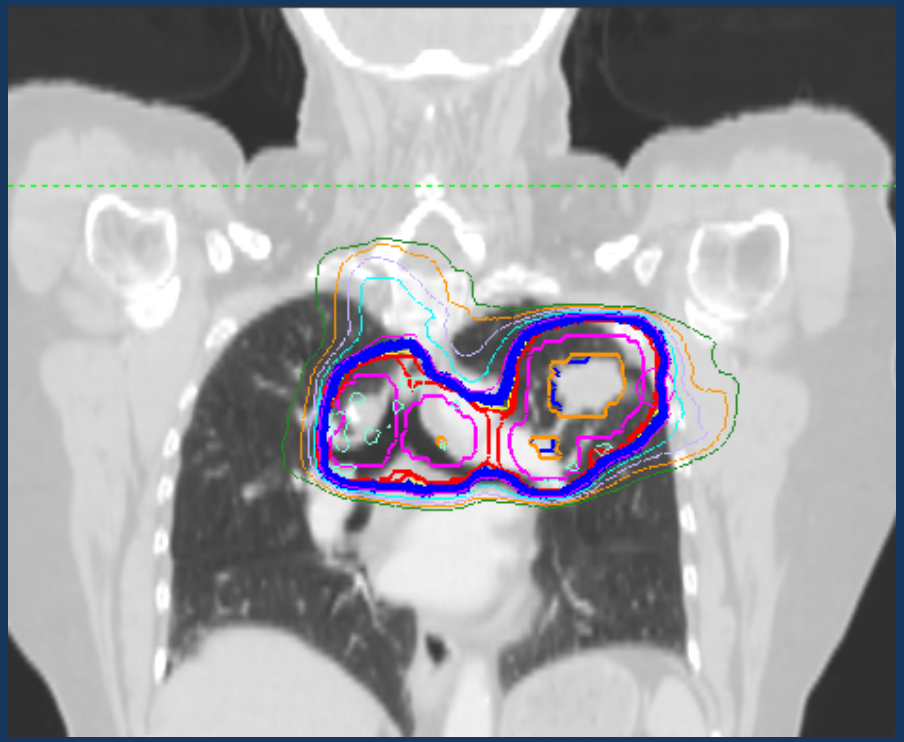


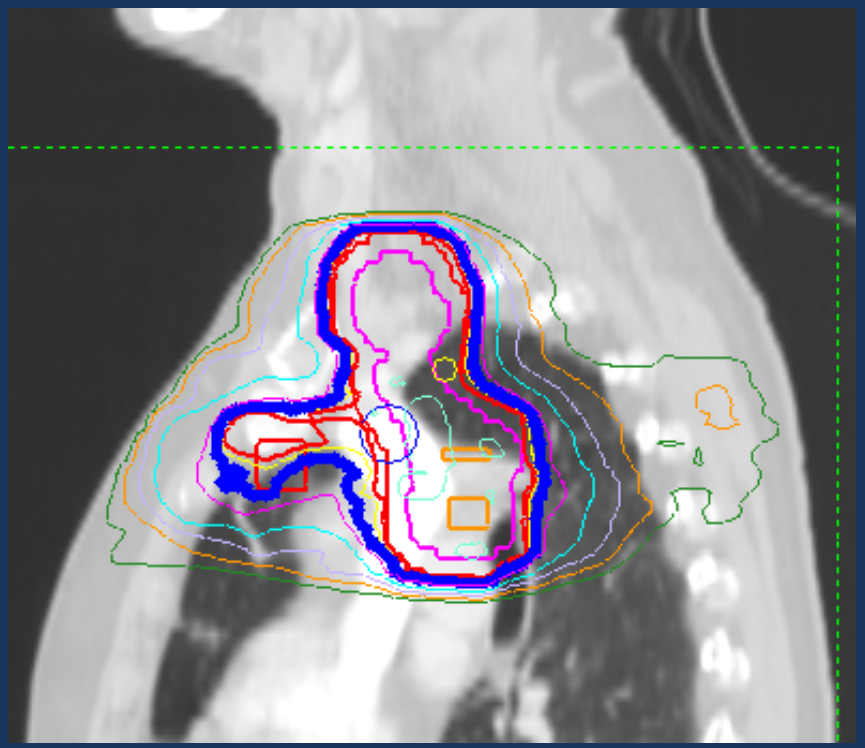


IMRT Planning: T2N3M0 adenocarcinoma

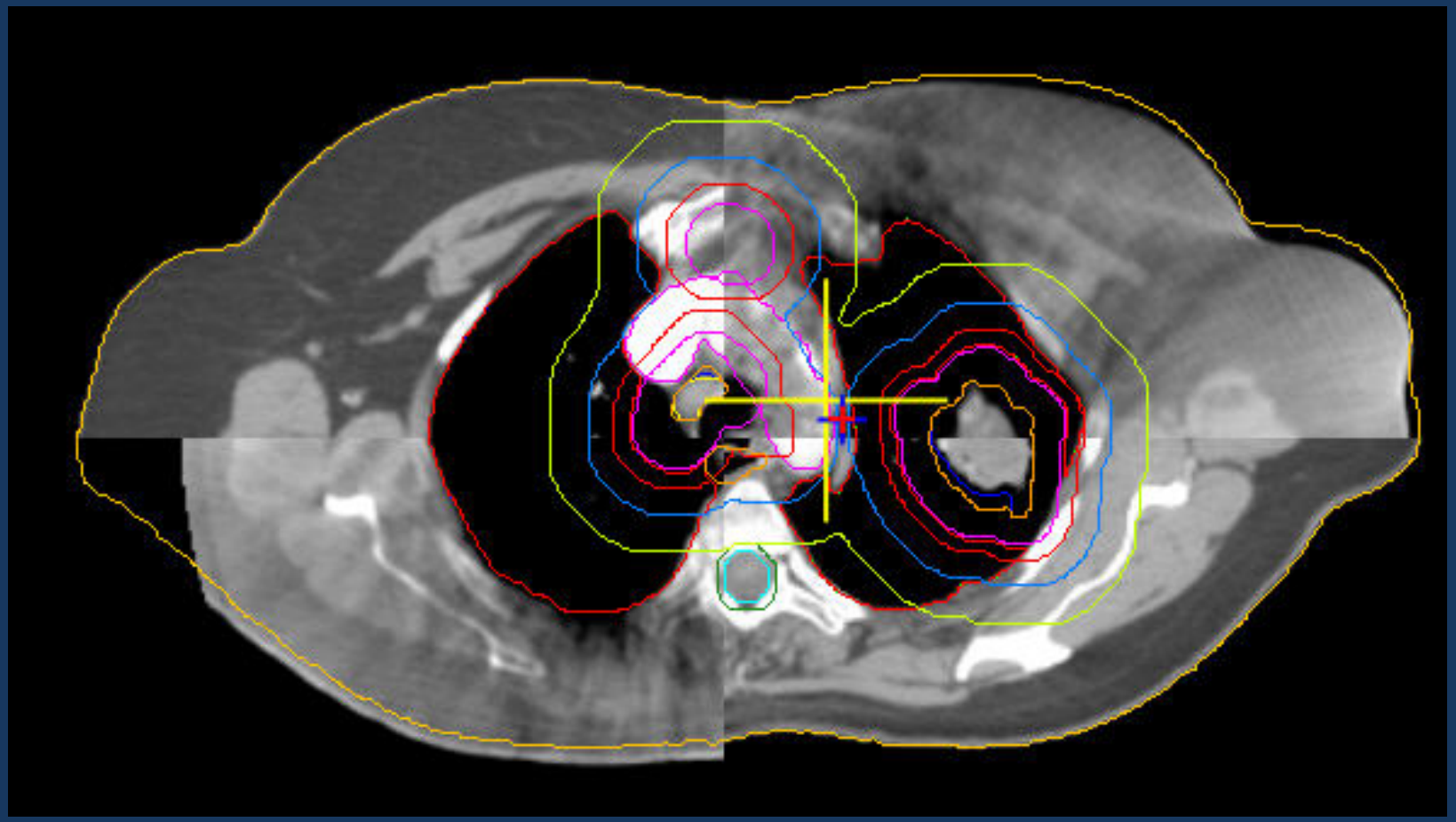


IMRT Planning: T2N3M0 adenocarcinoma





Daily Image Guidance: CBCT



Potential Side Effects of Thoracic Radiotherapy

- Lungs
  - Inflammation
  - Scarring
  - Decreased pulmonary function
- Heart
  - Pericarditis
  - Scarring/valve damage/increased risk of MI or cardiac death
- Spinal Cord
  - Myelopathy
- Esophagus
  - Esophagitis
  - Scarring
- Radiation-induced cancers

Reducing Toxicity for Locally Advanced Lung Cancer

- Pneumonitis
  - Major complication of RT for lung cancer
  - Recent pooled analysis suggests ~30% rate of symptomatic pneumonitis following CRT for stage III NSCLC (Palma et al, 2013)
  - Highest risk groups include elderly and those receiving concurrent carbo/taxol

Approaches to reducing pneumonitis risk

- Reduced margins for setup error and internal motion
  - Daily image guidance
  - Motion management (compression or gating)
  - RT to elective nodal regions is now infrequently used as isolated nodal failure is rare

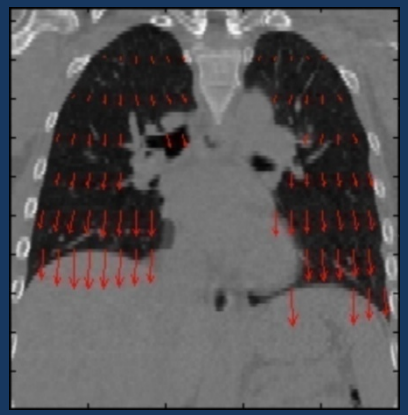
Emerging Approaches to reducing pneumonitis risk

- Identification and selective avoidance of high-functioning lung sub-regions
  - 4D CT
  - SPECT
  - Other functional imaging techniques

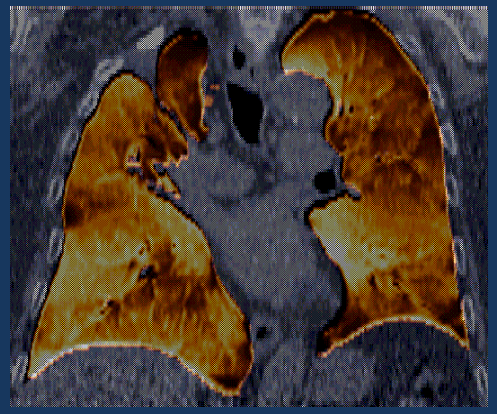
4DCT Functional Lung Avoidance

4D CT image

Displacement vector field



Ventilation image



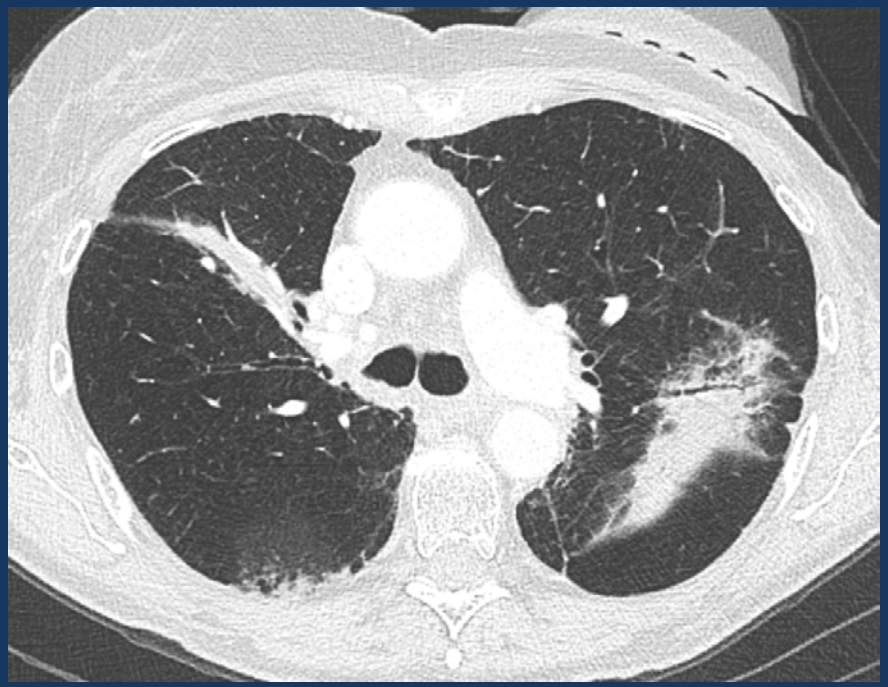
Deformable image registration (DIR)

Quantification of regional volume change

Slide courtesy of T. Yamamoto PhD, UC Davis

Treatment of Radiation Pneumonitis

- Long prednisone taper is standard for dyspnea
  - 5-6 weeks, starting at 20 mg TID with rapid fall off



Radiotherapy for metastatic lung cancer

- Palliation of painful bone metastases
  - 1-10 fractions
- Brain metastases
  - Gamma knife (~1-4 lesions)
  - Whole brain radiation (~30 Gy in 10 fractions)
- SBRT for oligometastatic disease in good performance status patients (investigational)

Conclusions

- Radiotherapy plays an important role in the management of lung cancer
  - SBRT is a standard option for early stage, medically inoperable disease
  - Concurrent or sequential chemoradiation for locally advanced disease
    - Studies are evaluating ways of reducing side effects for these patients
  - Palliation
    - Bone mets, brain mets, airway obstruction, SVC syndrome

Thank you!

Feel free to email me with additional questions

medaly@ucdavis.edu