LUNG CANCER AND LIVER CANCER

Recent advances in management

Alexander Geng MD
Medical Director
San Francisco CyberKnife Radiosurgery Center
St Francis Memorial Hospital
DISCLOSURES

- None
Rationale of these choices

Part I – Lung Cancer
  - Epidemiology of lung cancer
  - Impact of screening
  - Advances in curing early stage lung cancer

Part II – Liver cancer
  - Primary liver cancer or HCC (hepatocellular carcinoma)
  - Secondary liver cancer or metastases to the liver
  - Role of Hepatitis in HCC
  - Epidemiology
  - Advances in managing liver cancer
Part I: Early Stage Lung Cancer: Recent advances from screening to treatment

Alexander Geng MD
Medical Director
San Francisco CyberKnife Radiosurgery Center
St Francis Memorial Hospital
INTRODUCTION

Topics

- Stage I Non-Small Cell Lung Cancer
- Lung cancer screening
- Stereotactic Ablative Radiotherapy vs. Surgery

Topics not covered

- Locally advanced and metastatic lung cancer (Stage III/IV)
- Small cell lung cancer
National data:
- 230,000 cases a year in the US
- 160,000 deaths annually
- Mortality greater than breast, colon and prostate cancer combined
- Median Age 70
- 1/13 for men and 1/16 for women lifetime risk

Historical Outcome
- Stage I-II 5 year OS 15.9% (Goldstraw J Thora Onc 2007)
Histology:
- Adenocarcinoma on the rise 50%
- Squamous cell cancer declining 35%
- Large cell 15%

Risk factors:
- Tobacco: 20x risk in current vs. 9x risk in former smokers
- Radon
- Asbestos
- Organics and metals, usually occupational

Stage on presentation
- Historically 1/3 presents with metastatic disease
- 40-50% with Stage II and III disease
- Stage I is most curable but also disproportionately small
LUNG CANCER SCREENING: CONTROVERSIES

- **Chest X-Ray screening:**
  - 6 RCT trials failed to show a survival benefit

- **CT screening**
  - National Lung Cancer Screening Trial (NEJM 2011): prospective RCT
  - Annual low dose CT vs. CXR for 3 years in high risk patients (53,000)
    - 55-79 years of age
    - 30 pack year or more
    - If former smoker, quit time within 15 years
  - Relative risk of Lung Cancer Death decreased by 20%
  - Relative risk of all cause mortality decrease of 6.7%

- The USPSTF issued a recommendation for CT screening in high risk populations
- 7 RCT trials ongoing in Europe: Only Nelson trial is large enough to show a mortality benefit
SCREENING: RESULTS FROM NLCST
- **Expected rise of lung cancer presentation in Stage I and II with screening**
- Smoking is on the decline in general in the bay area.
  - Significant percentage of current and former smokers in an older population
- In addition, adenoCA, least correlated with smoking is on the rise
- Most centers are capable of low dose screening CT
- Screening program must be in place for proper follow-up
STAGE I NSCLC - TREATMENT

- Historical Gold Standard: Lobectomy (94% local control/LC)
  - 5yr OS 70-80% (Martini J Thora Cardiovasc 1999)
    - Medically fit and younger population
    - 5-25% upstaged with mediastinal LND and excluded
  - Alternative: wedge resection and pneumonectomy
    - Wedge LC is 82%

- Can elderly and medically inoperable patients be observed?
  - Median survival ~1 year
  - Cancer specific death quite high
  - Stereotactic Ablative Radiotherapy (SABR)'s use originates here
THORACOTOMY AND LOBECTOMY
Surgical Techniques

- Pneumonectomy
- Sleeve lobectomy
- Wedge resection
- Lobectomy
- Segmentectomy
STEREOTACTIC ABLATIVE RADIOTHERAPY (SABR) CHARACTERISTICS

- Accounting for Motion
  - 4D Planning

- Small tumour volumes
  - Small margins

- Many Beam Directions
  - 7-11 Beams / Arc Therapy

- Steep dose gradients
  - Inhomogeneous target dose

- Accurate Targeting
  - CBCT pre-RT

- High dose per fraction
  - Short total treatment duration
RTOG 0236: a phase II prospective multicenter trial of SABR for early stage lung cancer

- 3 yr LC of 97%, 5yr LC of 93%: same as surgery
- 5yr OS 40%: much lower than surgery? And Why?
  - Age, pulmonary function, comorbidity: non-cancer deaths dominate
  - 5-25% upstaging at surgery vs. 0% with SABR
  - Propensity score matched analysis shows equivalent OS as surgery
- 5yr distant metastatic rate 15-25%: same as surgery
- No severe late toxicity or side effects

STAGE I LUNG CANCER: OUTCOME OF SABR
Stage I-II non-small-cell lung cancer treated using either stereotactic ablative radiotherapy (SABR) or lobectomy by video-assisted thoracoscopic surgery (VATS): outcomes of a propensity score-matched analysis


A. Locoregional control rates
B. Distant control rates

P = 0.037

P = 0.070

SABR VS. SURGERY: LOCOREGIONAL CONTROL
STAGE I LUNG CANCER: SABR VS. SURGERY

- SABR Outcome is equivalent or potentially even superior to surgery as seen in medically inoperable patients
- What is SABR’s outcome with operable patients
  - More than 4 prospective trials
  - Most closed early due to difficulty in patient accrual
  - Pooled analysis again shows excellent outcome
CYBERKNIFE SABR OPERATION
CT CHEST BEFORE SABR AND 3MO AFTER
SABR is an advanced technique of radiotherapy

- **Ablative dose of x-ray** to tumors in 1-5 treatments
  - Conventional RT 30-35 treatments of small doses of x-ray
- **High precision and accuracy of less than 1mm**
  - Conventional RT's margin of error is up to 5 to 10 times bigger
- CyberKnife is one of the platforms for Lung SABR
  - **Outpatient non-invasive** treatment for 1-1.5 hours a day for a few days
  - **Pain free**: no local or general anesthesia
  - **Normal breathing** throughout treatment delivery tracked by the robot

SABR originally emerged as a treatment for

- Medically inoperable/elderly patients
- Patients who refuse surgery
- Early stage lung cancer is a **highly lethal but increasingly curable** disease
- Both surgery and Stereotactic Ablative Radiotherapy (SABR) are curative modalities
  - SABR is non-invasive, non-operative, completely outpatient and pain-free
  - Clinical trials show **equivalence in survival and tumor control between surgery and SABR**
- SABR has demonstrated superior survival outcome in medically inoperable early stage lung cancer patients
- Emerging data show equivalence of survival outcome compared with surgery in medically operable patients as well
- **Lung cancer** is complex disease that **requires a multi-disciplinary approach**
  - Thoracic surgery, medical oncology, radiation oncology, pathology and radiology are all crucial as a team to recommend the best course of action based on individual patient’s physiologic reserve and their tumor characteristics
Part II: Liver Cancer – A brief review in epidemiology and management

Alexander Geng MD
Medical Director
San Francisco CyberKnife Radiosurgery Center
St Francis Memorial Hospital
Liver cancer can be

- **Primary** (hepatocellular carcinoma) – HCC
  - Strong correlation with cirrhosis of any cause (viral, environmental, genetic diseases)
  - 3-5% per year conversion rate to HCC after cirrhosis
  - In the US, relatively low incidence (out of top 10) but high mortality (rank 9)
  - Relevance to the Chinese community
    - Much higher incidence of chronic hepatitis B and C than general population
    - Higher incidence of HCC as a result

- **Or secondary** (metastasis) from other cancers
  - Liver metastasis is very common
  - Incidence varies by primary cancer’s origin
    - Liver has a unique dual blood supply (portal venous and hepatic artery)
    - GI cancers and GYN cancers in particular have a high propensity of causing liver mets
  - Limited metastasis to liver alone is Stage IV but may still be potentially curable
Epidemiology

Cirrhosis

- Alcohol Liver Disease (29%)
- Metabolic: NAFLD...NASH (13%)
- Hereditary Hemochromatosis
- Chronic Hepatitis B (Most common cause worldwide)
- Chronic Hepatitis C (36%)

HCC

% from Mayo Clinic experience- Yang et al., Clin Gastroenterol Hepatol 2011
Hepatocellular Cancer: Incidence

Incidence rate tripled
Death rate doubled
Greatest proportional increase in cause of cancer-related deaths in the US
Obesity, increased Hep C infection incidence, and long latency period from infection to cancer development → likely major health problem for years to come

El-Serag and Kanwal
Hepatology 2014. Wiley

US INCIDENCE AND MORTALITY
Cirrhotic liver nodules

- Size > 1cm:
  - Imaging studies alone are sufficient for diagnosis – MRI or triple phase CT
  - Routine biopsy is not needed
- Size < 1cm: serial imaging follow-up, usually U/S q3months

Progostication Systems

- **Child Turcotte Pugh system**: class A/B/C predictive of survival
  - Sometimes referred to as Child-Pugh score
- **ALBI** score: albumin and bilirubin based scoring system
- **Barcelona Clinic Liver Cancer stage (BCLC)**
- **AJCC** and other systems
Management

- Standard Potentially Curative Treatment
  - Partial hepatectomy (eligible < 20% at presentation)
  - Liver transplant
    - Milan criteria
      - single lesion ≤5 cm, up to 3 lesions, none > 3 cm
      - No gross vascular invasion, no nodal or distant metastases
      - four-year survival rate of 75 percent could be achieved

Dawson LA, Sem Rad Onc 2011

STANDARD CURATIVE APPROACH
Resection vs. Transplant

- Survival similar in observational series, no randomized data
- Resection will see up to 80% recurrence due to underlying cirrhosis
- Transplant’s recurrence rates are 8% (Milan data)
- < 20% patients are eligible for resection or transplant

How do we help the other 80% of HCC patients?
Radiofrequency ablation (RFA)
- Microwave cooking the tumor
- Thermal ablation
- Good tumor control for small lesions but ineffective for large tumors

Transarterial ChemoEmbolization (TACE):
- Alter blood supply
- Chemotherapy
- Eligibility limited by vascular anatomy, liver reserve and medical comorbidities

Transarterial RadioEmbolization (TARE):
- Alter blood supply
- Internal irradiation of the tumor from inside out
- Eligibility limited by vascular anatomy, liver reserve and medical comorbidities

Stereotactic Ablative Radiotherapy (SABR)
- High dose of X-ray in 1-5 sessions to obliterate tumors
- Limited by liver reserve only

MANAGEMENT – NON-SURGICAL
Characteristics

- Non-invasive, completely outpatient, pain- and anesthesia-free
- Local control 80-90%, superior to TACE
- Tumor motion tracking capability
  - Built-in CT scanner (Varian TrueBeam)
  - In-vivo real time tumor tracking (CyberKnife)
- Rapid sharp dose falloff limit toxicity to normal liver
- Tumor size does not matter
  - It’s not what’s ablated but what is left behind
  - 700cc of liver needs to be spared
SABR FOR LIVER CANCER
SABR FOR LIVER CANCER
SABR – PRE AND 3MO POST TREATMENT
Liver metastasis makes any cancer Stage IV
- Traditionally considered incurable
- Newer data show an oligometastatic state: potentially curable

Management
- Local therapy is effective: surgery, SABR
- RFA, TARE, TACE are also used
- SABR local control is affected by primary tumor histology
  - Lack of cirrhosis increases hepatic physiologic reserve
  - Higher ablative doses are possible
Liver cancer, either primary (HCC) or secondary (mets) is a complex disease state that requires a multi-disciplinary approach:

- Input of hepatology, surgery, radiation oncology, medical oncology, transplant, interventional and diagnostic radiology
- Careful patient selection and individualized treatment selection
- When available, enrollment in clinical trials is recommended

SABR is a non-invasive and potentially curative ablative technique that plays an important role in the management of HCC and liver metastases:

- SABR provides local control comparable to surgery
- Many platforms can deliver SABR: CyberKnife, TrueBeam, etc
- In properly selected cohorts, SABR shows minimal toxicity even in cirrhotic livers
- SABR’s current role
  - Used alone as a potentially curative modality
  - Or in “bridge therapy” or to downstage patients in order to convert patients to become transplant-eligible
THANK YOU FOR YOUR ATTENTION