CT imaging of Thymoma: Standardized Reporting

- Overview of
- Staging Thymoma
  - Goals of CT imaging/reporting in staging
    - Predictors of invasive disease
      - Direct Predictors
      - Indirect Predictors
  - Structured Reporting
    - What it means
    - When to use it
- Post treatment imaging
  - RECIST 1.1 and modified RECIST for pleura
  - Long term follow up

Thymoma

- Most common 1st neoplasm of anterior mediastinum
  - Increasing incidence after 40 y.o. until age 60
  - Male/female incidence approximately equal
- Relatively rare – 1% of thoracic neoplasms
  - 1-3/1,000,000
  - Literature based on retrospective single institution series
  - Varying definitions and outcomes over time and between institutions making comparison difficult
- The International Thymic Malignancy Interest Group (ITMIG) created to facilitate international collaboration
  - Standardize outcome measures
  - Standardize definitions

Thymoma Histologic Classification

- Current classification differentiates thymoma from thymic carcinoma
- Not clinically useful in predicting invasive disease
  - B3 vs A-B2 carries only modest increase risk of invasive disease
  - Grades A-B3 may be intermixed within the same tumor

Masaoka-Koga Staging

- Based on gross operative findings and microscopic invasive properties of the tumor
  - Final staging based on microscopy: demonstration of tumor cells crossing anatomical borders
- Correlates with outcome
- Used to guide thymoma treatment

Masaoka-Koga Staging

<table>
<thead>
<tr>
<th>Stage</th>
<th>Microscopically</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Completely encapsulated</td>
</tr>
<tr>
<td>II</td>
<td>(a) Microscopic invasion into capsule</td>
</tr>
<tr>
<td></td>
<td>(b) Macroscopic invasion into surrounding fatty tissue or grossly adherent but not breaking through mediastinal pleura or pericardium</td>
</tr>
<tr>
<td>III</td>
<td>Macroscopic invasion into neighboring organ (i.e., pericardium, great vessels, lung)</td>
</tr>
<tr>
<td>IV</td>
<td>(a) Pleural or pericardial dissemination</td>
</tr>
<tr>
<td></td>
<td>(b) Lymphogenous or hematogenous metastasis</td>
</tr>
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Adapted from Koga Pathol Int 1994
Thymoma Staging and Survival

<table>
<thead>
<tr>
<th>Stage</th>
<th>Complete Resection 5y</th>
<th>Overall Survival 10y</th>
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<tbody>
<tr>
<td>I</td>
<td>95-100%</td>
<td>90-100%</td>
</tr>
<tr>
<td></td>
<td>85-100%</td>
<td>75-90%</td>
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<tr>
<td>II</td>
<td>65-80%</td>
<td>50-70%</td>
</tr>
<tr>
<td>IV</td>
<td>30-50%</td>
<td>30-40%</td>
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</table>

Thymoma Treatment

- Based on Masaoka-Koga staging
  - Stage I - Surgery only
  - Stage II - Surgery. Postoperative radiation incompletely resected tumors
  - Stage III-IVA – If identified preoperatively, should receive chemotherapy prior to surgery as it improves survival
  - Stage IVB – Chemotherapy is recommended

Macroscopic Invasion into neighboring organs (Direct Signs)

- Vascular involvement
  - Irregular luminal contour
  - Endoluminal soft tissue
    - Direct extension of the tumor into the vessel lumen
    - Intravascular component similar in attenuation and enhancement as bulk of the primary mass
  - Vessel Encasement

Indirect Signs of Invasive (≥ Stage II) Disease

<table>
<thead>
<tr>
<th>Tomyama JCAT 2001</th>
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</thead>
<tbody>
<tr>
<td>50 patients: 27 invasive, 23 non invasive:</td>
</tr>
<tr>
<td>Lobulated</td>
</tr>
<tr>
<td>Irregular</td>
</tr>
<tr>
<td>Low attenuation</td>
</tr>
<tr>
<td>Calcification</td>
</tr>
</tbody>
</table>
Predictors > Stage II
Evaluated at MD Anderson

- Tumor Size > 7 cm
- Prior study showing 8-11 cm diameter a predictor
- Calcifications
- Roundness
- Fat planes
- Infiltration of surrounding fat
- Adjacent Lung changes
- Any Pleural effusion
- Lymphadenopathy
- Pulmonary nodules
- Vessel abutment > 50%

Predictors > Stage II Selected by Multivariate Regression at MD Anderson

- Tumor Size > 7 cm
- Prior study showing 8-11 cm diameter a predictor
- Calcifications
- Roundness (absent lobulation)
- Preservation of fat planes
- Infiltration of surrounding fat
- Adjacent Lung changes
- Any Pleural effusion
- Lymphadenopathy
- Pulmonary nodules
- Vessel abutment > 50%

Findings to Include in Standardized Report

- Direct Findings
  - Endovascular mass or irregular vessel lumen
  - Vessel encasement
  - Pleural or pericardial involvement
- Indirect signs
  - Tumor Size > 7 cm
  - Roundness (absent lobulation)
  - Infiltration of surrounding fat

Terms: Size (Indirect Signs)

- Document size in three axes
- The axial slice chosen for measurement is that which demonstrates the longest tumor dimension
- The short axis is perpendicular to the long axis on that same slice
- Superior-inferior dimension should be obtained by subtracting the lowest from the highest bed position in which the primary tumor is seen
- Rather than utilizing single coronal reconstruction

Terms: Contour (Indirect Signs)

- Smooth: absence of spiculation, ill-defined borders or lobulation
  - Smooth lesions are typically spherical or ovoid in shape, but lesion contours may also conform to the shape of the adjacent mediastinum
  - Lobulated contour is one that exhibits one or more lobulations
  - Convex tumor contours with adjacent notches between tumor lobules

Terms: Infiltration (Indirect Signs)

- Infiltration of fat in one interface is sufficient to constitute positive finding:
  - Some areas of tumor may demonstrate well defined borders
  - Tumor abutment against mediastinal vessels without an intervening fat plane is not (by itself) considered as infiltrating
Predictors studied at MD Anderson

- Tumor Size > 7 cm
  - Prior study showing 8-11 cm diameter a predictor
- Infiltration of surrounding fat
  - Adjacent Lung changes
- Roundness (absent lobulation)
- Preservation of fat planes
- Calcifications
- Roundness (absent lobulation)
- Vessel abutment > 50%

Stepwise Multivariate Regression

- Variables added to or subtracted from the equation until improvement in prediction falls below a selected threshold
- Data can be over-fitted - i.e. spurious variables included that improve prediction only for the sample used to generate the equation (add noise).
  - Prediction rule less effective in different group of patients
- Generating equation can exclude variables that actually do improve prediction (add signal)

Stepwise Multivariate Regression

- Two reasons a variable may be excluded from multivariable equation
  - Variable has poor correlation with outcome (e.g. invasive disease)
  - Variable correlates well with outcome but is highly correlated with another variable that has a higher correlation and is entered into the equation first
- It is NOT correct to say that variables excluded from regression analysis “are not associated” with the outcome variable

Indirect Findings for Standardized Report

- Vessel abutment = percentage of the vessel circumference contacts the tumor without an intervening tissue plane
  - >50% circumference predicts invasive disease
- Heterogeneous attenuation is associated with invasive stage
  - Heterogeneity pre or post IV contrast favors invasion*
  - Cystic component may be independent predictor*

Terms: Vascular abutment, Heterogeneity (Indirect Signs)

- Calcifications can be curvilinear, punctate or coarse
- HU > blood pool with exception of IVC and tracheocephalic vein on side of injection
- Smallest increase in Odds Ratio of CT predictors 2.45 (1.02-5.89)
- Recent review argues against utility in staging
  - Harris Wohl J of Surg Oncology 2011

Terms: Calcifications (Indirect Signs)
Terms: Phrenic N. Involvement and Diaphragmatic Elevation

• Elevation of diaphragm
• If phrenic nerve involvement pre-operative chemotherapy may improve chance for complete resection
• Nerve travels posterior to subclavian veins, anterior to hila

Terms: Pleural Effusions and Lymphadenopathy

• Pleural effusions not common among patients with thymoma.
  - More frequently associated with thymic carcinoma and metastatic pleural involvement by primaries other than thymomas
• Enlarged mediastinal nodes seen on CT may be sampled preoperatively
  - Determine whether adjuvant chemotherapy needed
  - Nodes not routinely staged at surgery

Structured reporting - Basics

• Optimizes capture of radiology report information for retrieval and re-use
• Three components
  – I. General format – headings/paragraphs that delineate basic elements,
    - e.g. “findings”, “impressions”
    - Widespread use
  – II. Itemized reporting
    - Often by anatomic region
    - Common in voice recognition templates

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Radiology Langlotz 2009

CT Diagnosis of Anterior Mediastinal Masses N = 127

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Calc</th>
<th>Adenopathy</th>
<th>Cystic</th>
<th>Invasion</th>
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<tbody>
<tr>
<td>Thymoma</td>
<td>19%</td>
<td>2%</td>
<td>39%</td>
<td>38%</td>
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<tr>
<td>Malignant Germ</td>
<td>23%</td>
<td>23%</td>
<td>73%</td>
<td>85%</td>
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<td>Lymphoma</td>
<td>9%</td>
<td>68%</td>
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Tomiyama Eur Journal or Rad 2009

ITMIG Prospective Project – Pre-treatment Prognostic Factors

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<tr>
<th>Size by CT findings (cm): X x Y x Z</th>
<th>Contour</th>
<th>Smooth</th>
<th>Lobulated</th>
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Radiology Langlotz 2009
Predicting Thymoma from CT

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<tr>
<th>Proven dx</th>
<th>First Choice</th>
<th>High Confidence</th>
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<tr>
<td>Thymoma</td>
<td>83%</td>
<td>72%</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>55%</td>
<td>94%</td>
</tr>
<tr>
<td>Mature Teratoma</td>
<td>58%</td>
<td>82%</td>
</tr>
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<td>Malignant Germ Cell</td>
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<td>50%</td>
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Tomiyama, Eur Journal Radiology 2009

Predicting Thymoma from CT

• On pre-biopsy imaging it can be difficult to distinguish non-thymic mediastinal masses from thymomas
  - Non-Hodgkins lymphoma > Hodgkins
• May be warranted to use thymic template if tissue diagnosis is unknown

RECIST : Everyday Structured Reporting

• Lymph Nodes
  - Short axis - perpendicular to longest diameter
  - < 10 mm normal
  - < 15 nontarget lesions
  - ≥ 15 mm target lesion
• Peripheral enhancement of nodes and masses
  - Include enhancing rim included
  - No adjustment for necrotic center

Eisenhauer Eur J Cancer 45:228-47, 2009

RECIST 1.1 Pleural Tumor

• Maximum of 5 measurements
• No more than two per organ
  - Rind Like masses, measure longest diameter along the chest wall

Modified RECIST Pleura Tumor

• Unidimensional measurements perpendicular to chest wall or mediastinum
  - Two sites at three different levels
  - Slices at least 1 cm apart
  - Sum of 6 sites = one univariate measurement
Recurrent Thymoma

- Late recurrence can occur even 5 or 10 years after resection and is not uncommon
- Surgery, when possible, remains the preferred therapeutic option
- Resection of recurrence improves survival

Pleural recurrence of thymoma

Thymoma Follow up Imaging

ITMIG Follow-up recommendations

- Chest CT scan yearly for 5 years after surgical resection
- After 5 years alternate chest radiograph and chest CT annually for up to 11 years
- After 11 years: annual chest radiograph only
- Chest CT every 6 months for 3 years in cases of:
  - Stage III or IVa
  - Incomplete tumor resection

Conclusions

- Goal of imaging is to predict tumor staging, in particular to identify > Stage II tumors
- Prediction depends on identifying both direct and indirect imaging findings of invasion
- Standardized reporting can facilitate data collection by ITMIG and potentially refine our use indirect findings
- Data collection may benefit from use of these descriptors widely among anterior mediastinal tumors
- Unique characteristics of thymoma warrant modification of RECIST 1.1 and long term imaging follow up