THE HUNT FOR METASTATIC DISEASE: USE OF IMAGING FOR STAGING CANCER AND ONCOLOGICAL SURGICAL PLANNING, SPECIFICALLY OF THE THORAX

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Role of diagnostic imaging in oncology
- identify primary and metastatic lesions
- monitor lesions
- facilitate diagnostic sampling
- assist surgical planning

Imaging modalities

Radiography
- Readily available, inexpensive, baseline screening test.
- Thoracic radiography is the mainstay to screen for pulmonary metastases.
- Abdominal radiography complements ultrasound and provides a global overview about relative size and location of organs.

Ultrasound
- Readily available, relatively inexpensive.
- Better characterisation of organs compared to radiography but poor specificity for disease processes, and sampling of tissue still required for diagnosis.
- Highly user-dependent.
- In dogs over 25 kg, abdominal CT is able to detect more lesions and more clinically relevant lesions than abdominal US and should be the preferred imaging modality in these larger patients. (Fields 2012)
- Limited use in the thorax - heart, parts of mediastinum, thoracic wall, pleural effusions, peripheral pulmonary lesions.
- Very easy to perform ultrasound guided sampling.

Computed tomography
- More expensive, may require anaesthesia.
- Better soft tissue contrast compared to radiography.
- Elimination of superimposition can make interpretation easier.
- Larger field of view compared to ultrasound allows formation of a global overview, particularly useful for large and complex lesions.
- Thoracic CT usually provides additional useful information compared to thoracic radiography, and often leads to a change in diagnosis. (Prather 2005)
- Use of multiplanar reformations and 3-dimensional modeling improves speed of interpretation, (Mang 2011, McMenamin 2015), accuracy (Berg 1998, Ferencik 2007), and diagnostic confidence (Chooi 2005).
- More sensitive for bone loss, more sensitive for pulmonary change including identification of nodules (Nemanic 2006)
- ‘Whole body CT’ to screen for primary and metastatic neoplasia?
  - increased radiation dose to patient
  - decreased accuracy of interpretation with increased number of images to review (Andriole 2011, Lee 2013)
  - how to interpret the ‘incidentaloma’?
• sampling of tissue still required for diagnosis
  in some cases, scintigraphy (Oblak 2013) or PET/CT (Seiler 2015) may be more appropriate
• CT-guided biopsy
  • Useful to target deep lesions or contrast-enhancing (‘viable’) tissue (Tidwell 1994).
  • In a case series of CT-guided sampling of thoracic lesions in 30 cats and dogs, complications
    of pneumothorax & pulmonary haemorrhage occurred in 43% of patients, but all
    complications were mild and clinically silent. (Zekas 2005)
  • A smaller case series of 14 dogs and cats with CT-guided sampling of lung lesions found that
    a clinical diagnosis was reached in all cases that had a biopsy, but only 80% of cases that had
    FNA. Although minor pneumothorax and bleeding were noted in some cases, no clinical signs
    were associated with these complications. (Yoshida 2007)
• CT data often used for radiation therapy planning (may be fused to MRI data).

Nuclear Scintigraphy
• Limited availability, produces planar (two-dimensional) images.
• Images physiologic processes.
• High sensitivity (depending on selection of appropriate radiopharmaceutical) but poor specificity.
• Able to provide both functional and morphologic information, but has poor anatomic detail.
• Generally, animals must be hospitalised until radiation emission returns to safe levels.

Magnetic Resonance Imaging
• Limited availability, relatively expensive.
• Excellent sensitivity for soft tissue lesions; often useful to identify tumour margins prior to
  surgery or radiation therapy.
• May over-estimate tumour size due to adjacent inflammatory change.
• Variable quality of images (magnetic field strength, operator expertise, available coils).
• Studies can be time-consuming to acquire, requires general anaesthesia.
• Difficulties in imaging thorax:
  • aerated lung - deficiency of mobile protons (water) returns no signal
  • air-soft tissue interface artefacts
  • motion blur (respiratory, cardiac, pulsatile blood flow) may be partially mitigated using
    techniques such as respiratory and cardiac gating.
  • CT tends to be preferred over MRI for advanced imaging of the thorax.

Future developments

Improved use of thoracic CT
• More research needed!
  • Larger case series leading to better knowledge about characterising specific tumours based on
    CT appearance.
  • Better lesion characterisation using dynamic CT and three-phase CT
• Fusion of CT and ultrasound for ultrasound-guided sampling, based on CT images

SPECT
• Single Photon Emission Computed Tomography
• Similar to Nuclear Scintigraphy, but rotating the detector about the patient generates a 3D
  rendering of the structure of interest.
• More accurately depicts distribution of radiopharmaceutical, but still has poor anatomic detail.
• Described in dogs with neoplasia (Whittemore 2004), but also in the investigation of myocardial
  perfusion and epilepsy in dogs.
**PET and PET/CT**

- Positron emission tomography
- Often uses ‘FDG’: 2-deoxy-2-[18F]fluoro-D-glucose - relies on excessive glucose utilisation by metabolically active tissue, including tumours and inflammation.
- Routinely used in human oncology for detection of cancer, staging and monitoring.
- Limited availability in veterinary medicine: largely experimental or small case series (Lawrence 2010, Seiler 2015).
- Poor anatomic detail of PET is overcome by simultaneous acquisition of CT, and image fusion of PET and CT data.

**Molecular imaging**

- Tailored contrast agents or monoclonal antibodies, targeting specific molecules.
- Typically used in MRI or nuclear imaging (scintigraphy, SPECT, PET).
- Magnetic Resonance Spectroscopy (MRS) (Lynch 2014) available in some high-field strength MRI units.
- Potential to allow specific tissue diagnosis.

**Screening for pulmonary metastases**

**Thoracic radiography**

- Commonly employed, but is not as sensitive as thoracic CT.
- Three-view thoracic radiographs are preferred over two-view.
  - dependent lung rapidly develops atelectasis and obscures lesions
  - superimposition of mediastinal structures can obscure lesions
  - eliminating one view from a three-view study would have changed the diagnosis in 12 to 15% of patients (Ober 2006)
- Ensure lungs are well inflated; if patient is anaesthetised, radiograph soon after induction and use positive pressure ventilation to inflate the lungs.
- Do not use digitized thoracic radiographs - loss of image information means reduced ability to detect pulmonary nodules. (Armbrust 2005)
  - American College of Veterinary Radiology recommends interpretation of digital images be based on the DICOM format rather than jpeg or other compressed files.
- Computed radiography and film-screen radiography performed similarly in ability to detect pulmonary nodules. (Alexander 2012)
  - Size limit for detection of soft-tissue pulmonary nodules on a radiograph is 5mm diameter, with detection reliable at 7 - 9mm diameter. (Nemanic 2006)
  - Metastatic disease may also have unstructured interstitial pattern, or alveolar pattern.

**Computed tomography**

- Preferred modality to screen for pulmonary metastases
- Technical aspects:
  - Multi-row detector CT machines preferred over single-row detector machines
    - more rapid acquisition
    - no respiratory motion artefact
    - superior image quality
    - sub-mm slice thickness, isovolumetric voxels
    - MPRs without ‘stair-stepping’ artefact
  - General anaesthesia with breath-hold techniques provide superior lung inflation and lesion detection; if breath-hold cannot be safely performed, then induce apnoea.
  - If dependent atelectasis is present, flip the patient, inflate using positive pressure ventilation, and repeat the scan.
• Acquire both pre- and post-contrast images.
• Single-row detector machine:
  • for best results in detection of pulmonary nodules, use a narrow collimation (3 to 5mm), pitch of 2 and reconstruction interval of 1 (Joly 2009)
  • consider high-resolution computed tomography (HRCT) protocols (Johnson 2004)
    • excellent spatial resolution but slow to acquire and usually cannot acquire through entire thorax, particularly useful for diffuse or interstitial lung disease
    • axial mode of acquisition
    • tightly collimated beam
    • high kVp and mA
    • decreased field of view
    • high spatial frequency reconstruction algorithm

• Detection of pulmonary nodules:
  • Compared to thoracic radiography, thoracic CT is able to detect smaller nodules (lower limit of detection approx 1mm diameter), more pulmonary nodules, and detect nodules in a greater number of lung lobes (Nemanic 2006, Eberle 2011, Armbrust 2012, Alexander 2012).
  • NOT ALL NODULES ARE METASTASES!
    • In humans, over 80% of pulmonary nodules identified in patients with extra-thoracic primary tumours were benign! (Chalmers 1991)
    • Guidelines for how to deal with small pulmonary nodules identified on thoracic CT in dogs with neoplasia are lacking, but in humans a repeat CT scan is recommended to monitor nodules for resolution or increase in size.
  • Note that linear measurements of nodule or mass size are much less accurate than volume measurements, and volume measurements are recommended for follow-up CT studies. (Revel 2004)

• Primary pulmonary neoplasia
  • Focal (mass or nodule) vs diffuse (ground-glass appearance)
  • Concurrent tracheobronchial lymph node (TBLN) abnormalities suggest pulmonary neoplasia; CT had a positive predictive value of 100% and negative predictive value of 89% for detection of abnormal TBLNs (Paoloni 2006), which appear enlarged (>12mm transverse maximum LN diameter) and heterogenous or ring-like contrast enhancement (Ballegeer 2010).
  • In cats: (Aarsvold 2015)
    • occurs more often in the caudal lung lobes, with 49% in the right and 30% in the left caudal lung lobe.
    • CT features of primary pulmonary neoplasia:
      • mass in contact with visceral pleura (96%)
      • irregular margins (83%) but well-defined borders (79%)
      • bronchial compression (74%) or bronchial invasion (19%)
      • gas containing cavities (63%)
      • mineralisation (56%)
  • In dogs: (Marolf 2011)
    • 95% were solitary, located in both cranial and caudal lung lobes, in central or peripheral zones (rather than perihilar)
    • CT features of primary pulmonary neoplasia:
      • solitary, well circumscribed, bronchocentric mass with internal air bronchograms
      • narrowing and displacement of bronchi
      • mineralisation (16%)
      • tracheobronchial lymphadenopathy (21%)
      • mild to moderate heterogeneous contrast enhancement (65%)
References


Andriole KP et al. *Optimizing analysis, visualisation, and navigation of large image data sets: one 5000-section CT scan can ruin your whole day*. Radiology. 2011. 259(2):346-362


