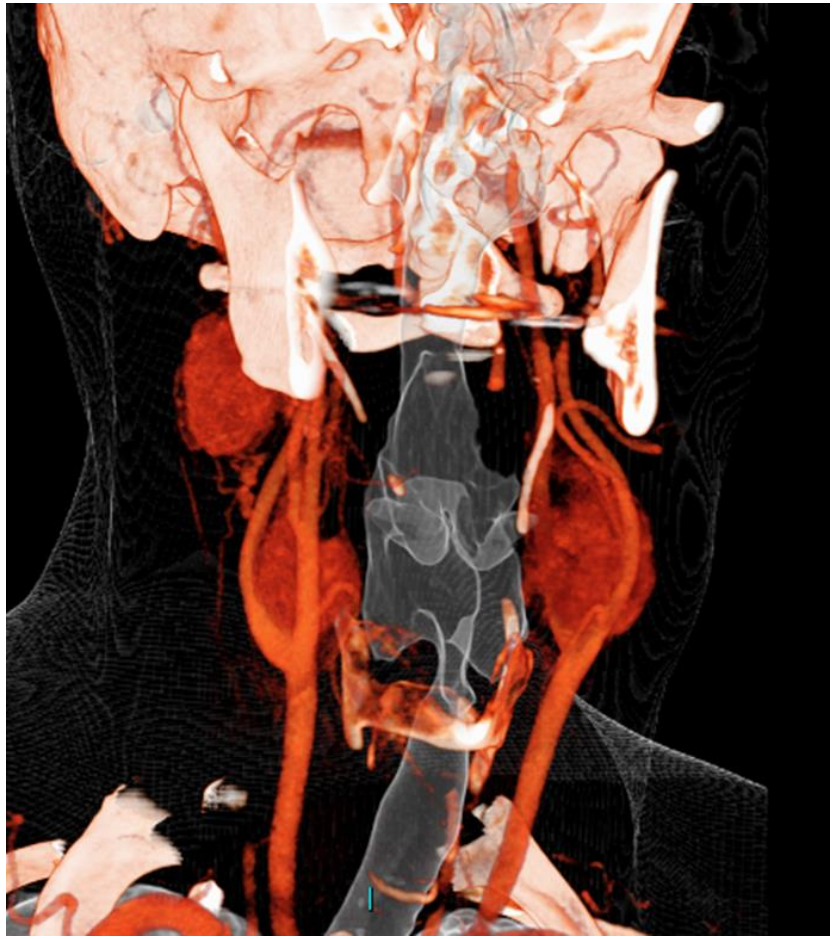
Guidelines on Management of Head and Neck Paragangliomas



Jonathan Smout

Liverpool Vascular Endovascular Service

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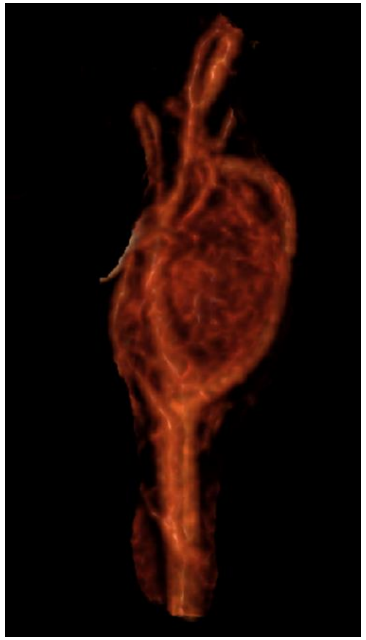
Paraganglionomas (ata)

- Derived from the embryonic neural crest (neuroendocrine tumour)
- Closely related to pheochromocytomas
- Incidence Head and Neck Paraganglionoma HNPGL of around 0.5 per million
- Peaks of 30 and 50 years (familial forms younger age).
- The WHO classification HNPGL
  - **Carotid body paraganglioma** - **CBT** (most common)
  - Jugulotympanic paraganglioma
  - Vagal paraganglioma
  - Laryngeal paraganglioma &
  - Miscellaneous



Natural History of HNPGL

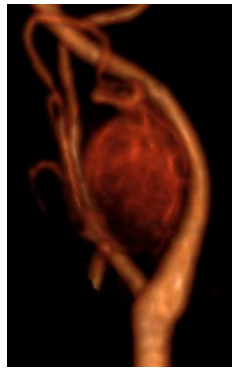
- MAJORITY - solitary, benign and slow growing
  - Often asymptomatic until large

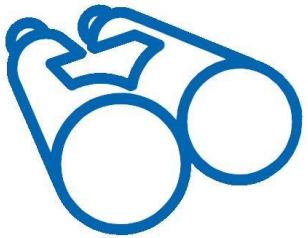
- MINORITY - more aggressive (genetic mutation)
  - Metastasize despite no differences in histological appearance

- Predictors of growth include:
  - Genetic status including positive family history (see below)
  - Age at presentation
  - Risk of malignancy is greater in Vagal PGLs > Carotid > jugular or tympanic PGLs.

Figure 3. Clinical appearance of a large carotid body tumor which had been slowly enlarging for forty-seven years.


Follow Up!





Guideline objectives

- These guidelines aim to provide succinct guidance for surgeons on the management of all forms of HNPGLs
- Summarises evidence
- Improve knowledge
- Standards for care

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- Call for participants 2017
- Consensus meeting 25th January 2018

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British Skull Base Society - Guidelines on Management of Head and Neck Paragangliomas (HNP)

- Otolaryngology
- Radiology
- Endocrine
- Vascular Surgery
- Neurosurgery
- Clinical Biochemistry
- Genetics
- Clinical Biochemistry
- Histopathology
- Nuclear Medicine
- Oncology

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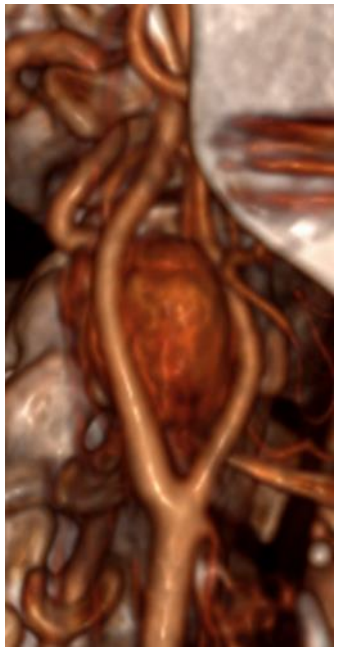

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Guideline recommendations
HNPGL

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Recommendations HNPGL:

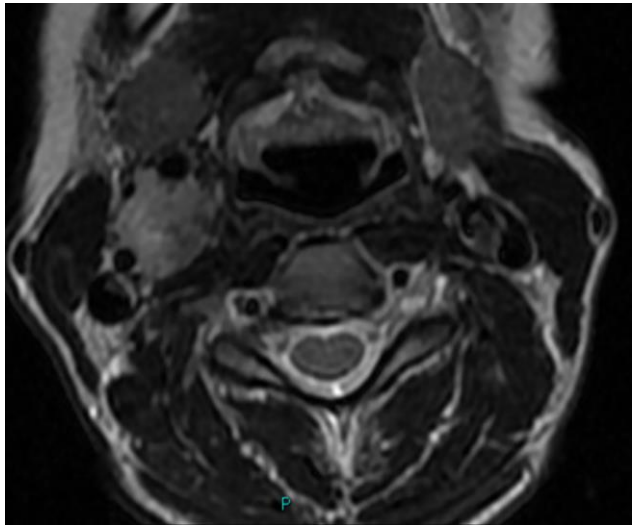
1. Establishing a dedicated MDT for the management of HNPGL

2. Otolaryngology assessment by a member of the MDT in all cases
   (Layrngoscopy / Tympanic assessment / DD's)

3. Endocrine assessment in all cases.
   (Plasma metanephrines at presentation)

4. Clinical genetics assessment in all cases.
   - The family history tumours - PGLs, phaeochromocytomas, renal cancer and gastrointestinal stromal tumours (GIST).

Recommendations HNPGL:



5. Imaging for Head and Neck PGL - HNPGL

- Contrast enhanced MRI of the head and neck
- Temporal bone PGLs (jugular and tympanic) CT of the skull base.
- MRI (CT) thorax, abdomen and pelvis

- 123Iodine labelled metaiodobenzylguanidine scintigraphy (MIBG) or Positron Emission Tomography (PET) optimal for metastatic disease
- **CTA pre- CBT surgery**

PGL associated gene abnormalities

Tumor syndrome	Gene	Locus	Inheritance	Head and neck	Thorax	Adrenal	Abdominal extra-adrenal	Malignancy risk
PGL1	*SDHD*	11q23	AD*	+++	+	++	++	+/−
PGL2	*SDHAF2*	11q13.1	AD*	++++	−	−	−	−
PGL3	*SDHC*	1q21	AD	++++	+/−	+/−	+/−	+/−
PGL4	*SDHB*	1p35-p36	AD	+	+/−	+	++	++
VHL	*VHL*	3p25.5	AD	+/−	+/−	++++	+	+/−
Familial pheochromocytoma syndrome†	*TMEM127*	2q11.2	AD	+/−	−	+++	+	−
Familial pheochromocytoma syndrome	*SDHA*	5p15.33	AD	++	+/−	+	+	+
MEN2†	*RET*	10q11.2	AD	+/−	−	+++	+/−	+/−
NF1†	*NF1*	17q11.2	AD	+/−	−	+	+/−	+
Familial pheochromocytoma syndrome†	*MAX*	14q23	AD*	+/−	+/−	++++	+/−	+/−

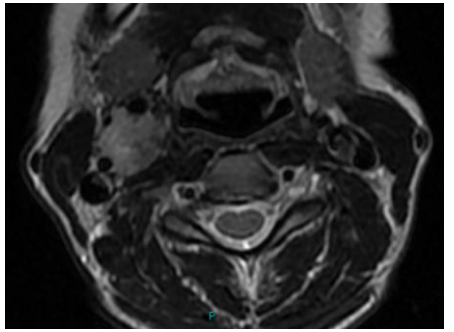
Abbreviations: PGL, paraganglioma syndrome; SDHD, succinate dehydrogenase subunit D; q, short arm of a chromosome; AD, autosomal dominant; SDHAF2, succinate dehydrogenase complex assembly factor 2 gene; SDHC, succinate dehydrogenase subunit C; SDHB, succinate dehydrogenase subunit B; p, long arm of a chromosome; VHL, von Hippel–Lindau syndrome; TMEM127, transmembrane protein 127; SDHA, succinate dehydrogenase subunit A; MEN2, multiple endocrine neoplasia type 2; NF1, neurofibromatosis 1; MAX, MYC-associated factor X.

*In SDHD, SDHAF2, and MAX mutations there is a parent-of-origin-dependant inheritance.

†HNPGs have very infrequently been described in patients with TMEM127,[80] MEN2,[23,43,44] NF1,[45] and MAX.[46]

- never reported; +/− <10%; + 10% to <30%; ++ 30% to <60%; +++ 60% to <90%; ++++ 90% to 100%.

Guidelines - Management options:



Initial management:

- Active surveillance with serial imaging +/- plasma metanephrines (MAJORITY)
- EXCEPT - Tympanic, jugular with nerve impairment, Secretory, malignant disease, rapid growth, patient choice)

Treatment options

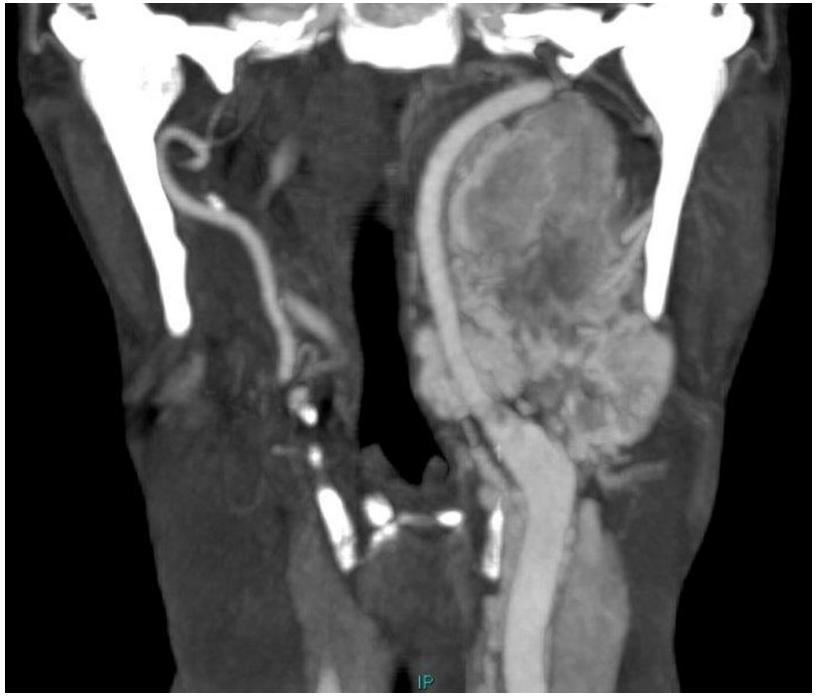
- Surgery
- Radiotherapy

Guidelines - Who to treat

- Tumours <4cm
  - A period of conservative management may be undertaken
  - Risk of growth following conservative management is high compared to surgical control rates and the lifetime risk of complications.
  - Control rates of surgery and radiotherapy are similar
    - ?Older age group who are less likely to develop long-term complications.
- Tumours >4cm
  - Because of the high-risk of complications when removing tumours larger than 4cm conservative management is often considered preferable in this group. Radiotherapy may be considered if there is tumour growth, especially in the older age group.

Surgical considerations

- Shamblin
- Cranial extent
- *CN's, Other lesions*



Carotid Body Tumor (Chemodectoma)

Clinicopathologic Analysis of Ninety Cases

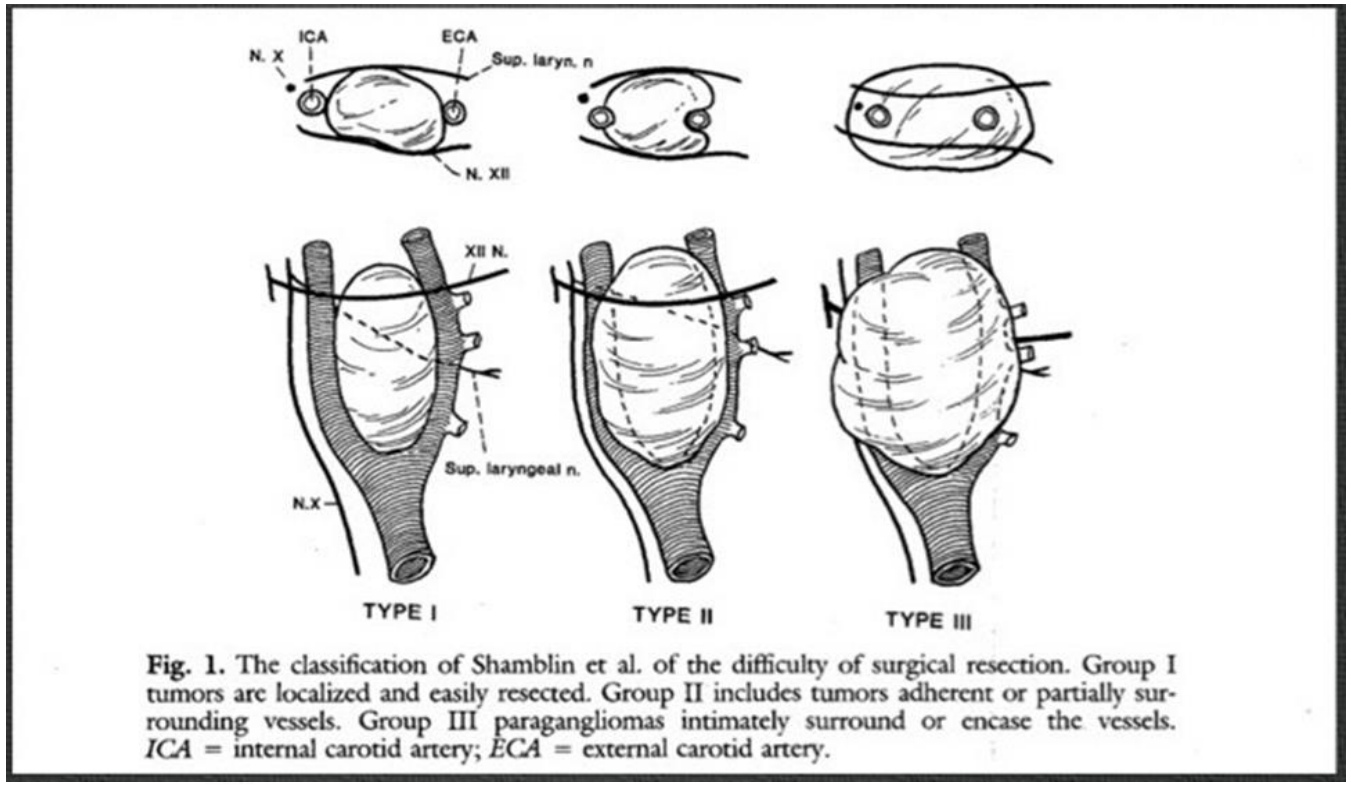
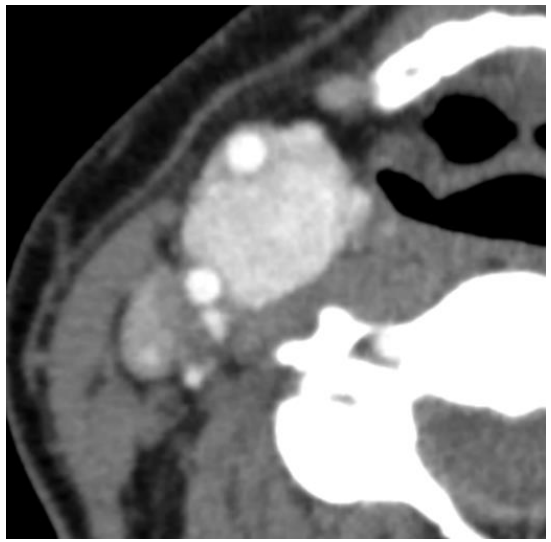
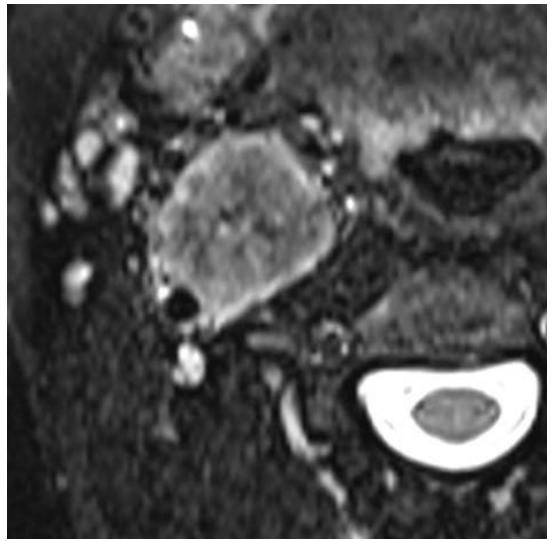
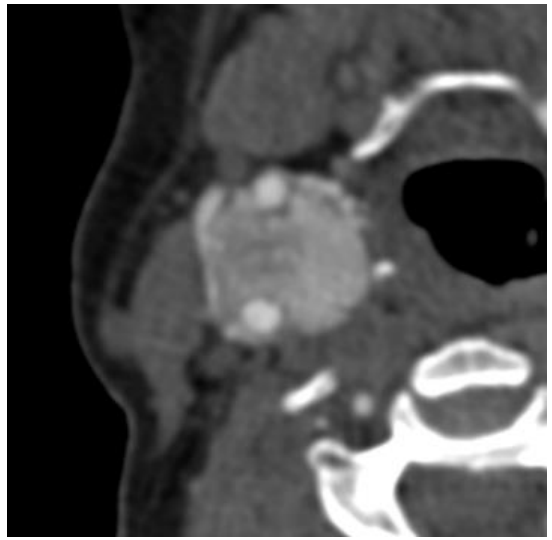
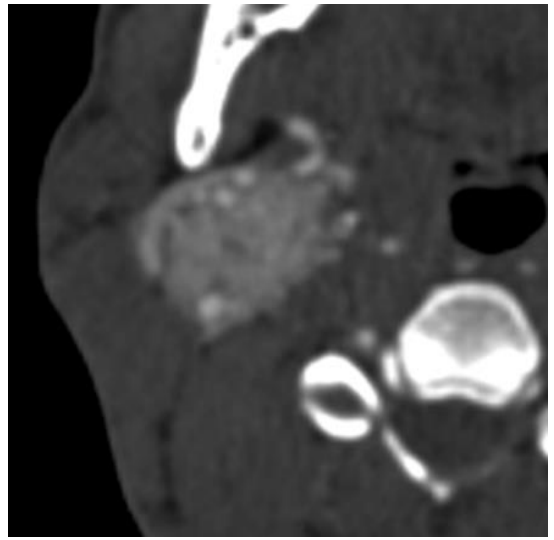


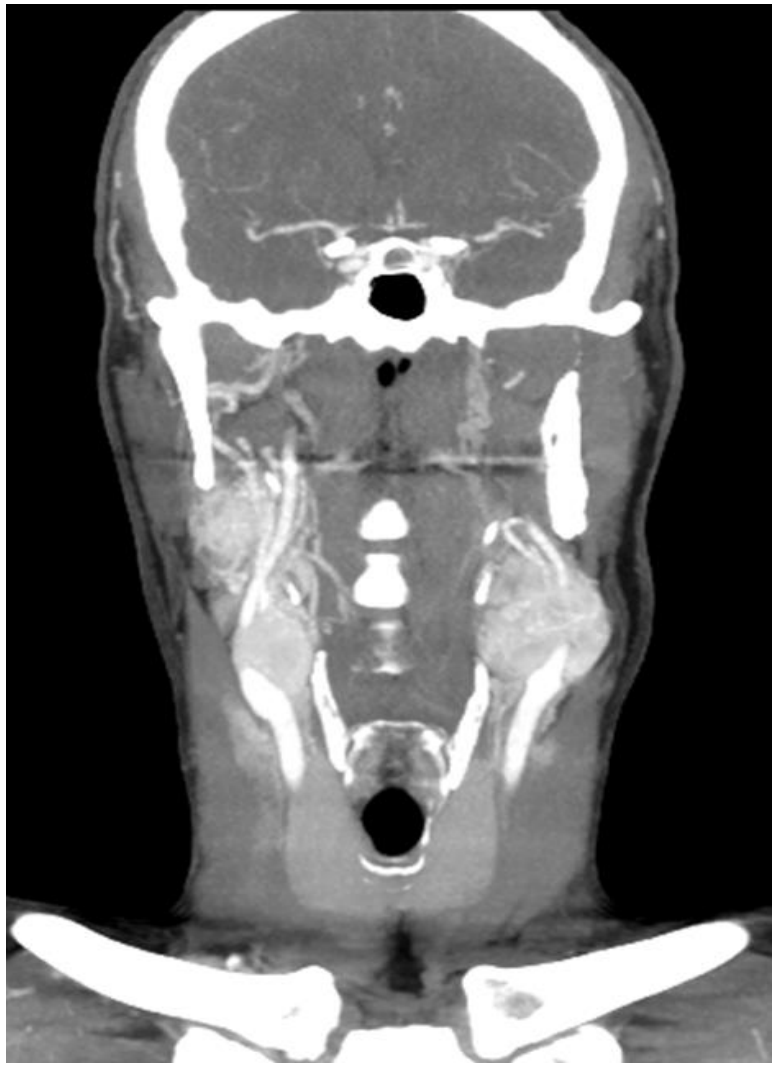
Fig. 1. The classification of Shamblin et al. of the difficulty of surgical resection. Group I tumors are localized and easily resected. Group II includes tumors adherent or partially surrounding vessels. Group III paragangliomas intimately surround or encase the vessels. *ICA* = internal carotid artery; *ECA* = external carotid artery.

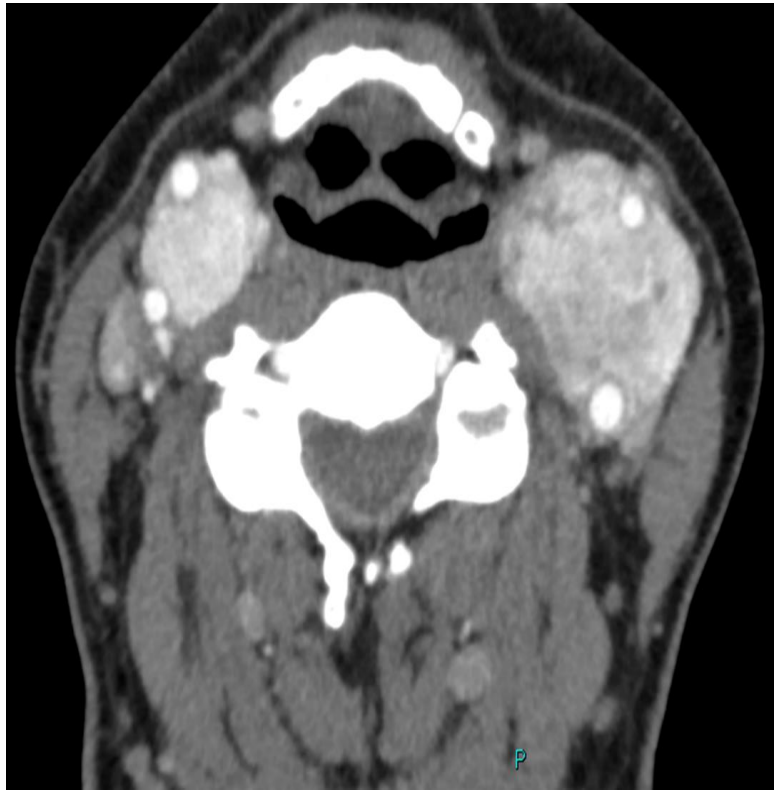
Shamblin Stage 2 → 3

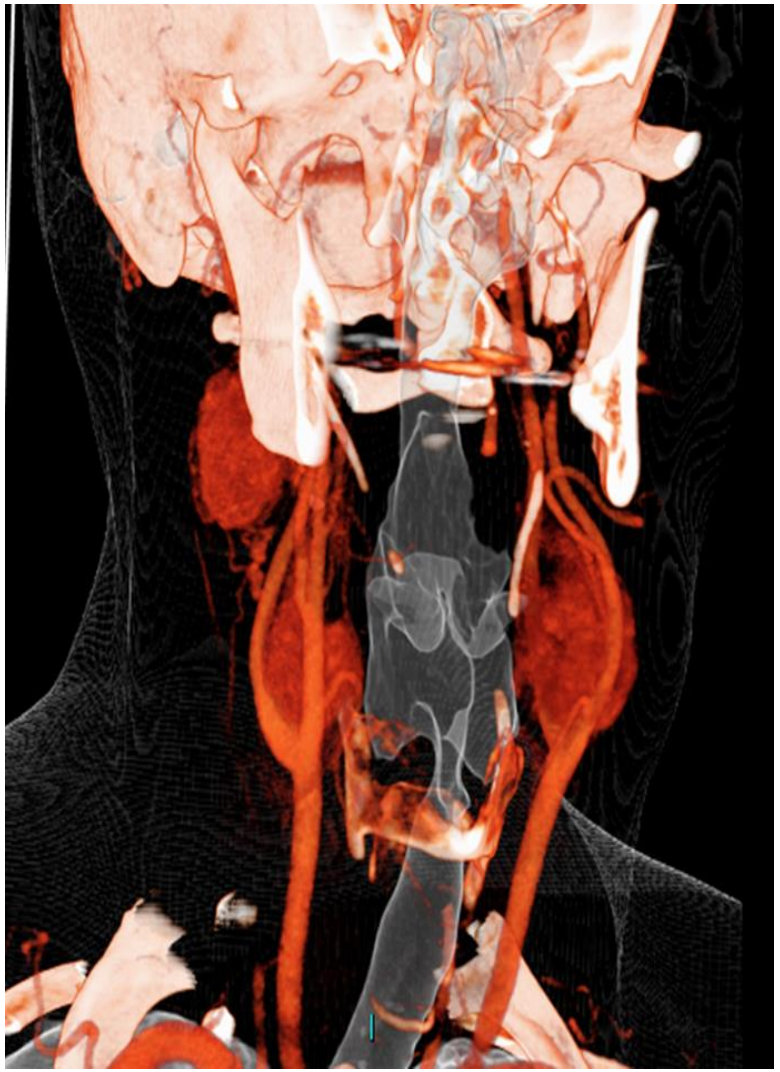





Shamblin 2.5?

CBT Case







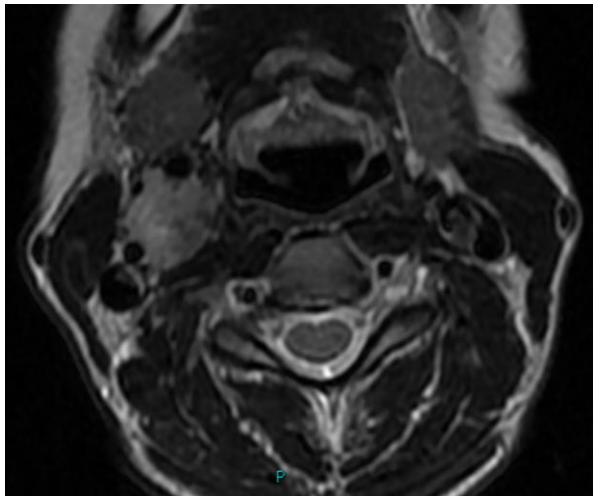
Our MDT

4 monthly meetings

Run by the existing Base of Skull team

- Radiology
- Otolaryngology
- Vascular Surgery
- Neurosurgery
- Histopathology
- Endocrine

- (Genetics)
- (Oncology)



Paraganglionoma referral

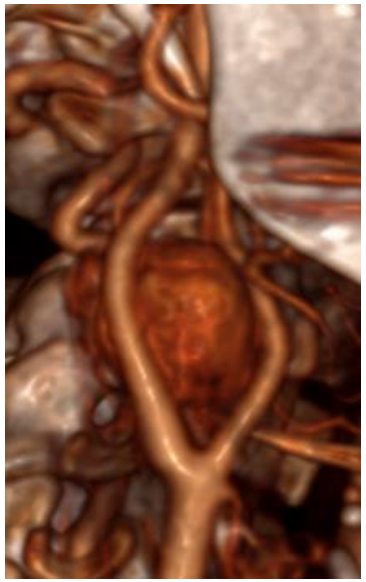
First Appointment
Serum metanephrine
Contrast MRI neck
ENT referral
Vascular (Carotid paraganglionoma)
Endocrine referral
Genetics referral

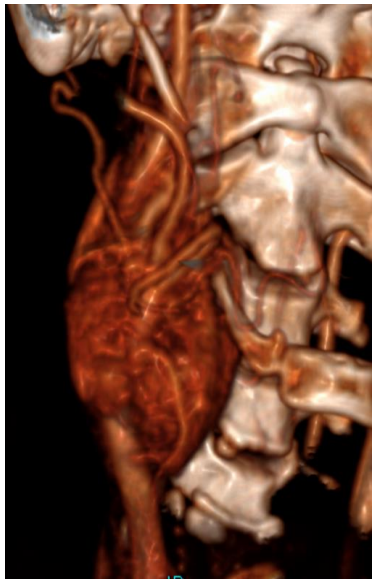
ENT	Vascular	Endocrine	Genetics
Layrngoscopy Tympanic assessmment	CBT's Surgically complex	Endocrine assessment and abdominal imaging	Counselling and relevant genetic tests

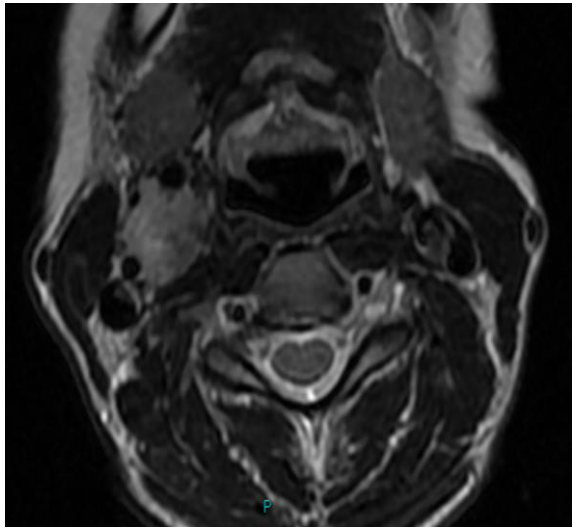
MDT Review

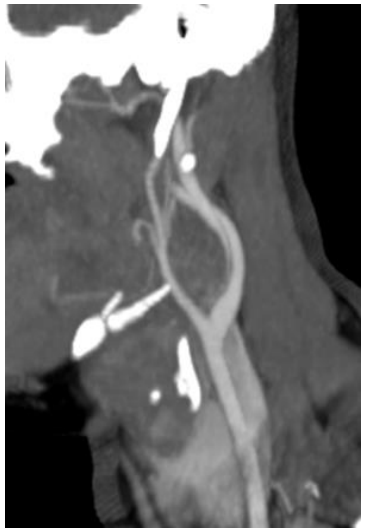
Conclusions

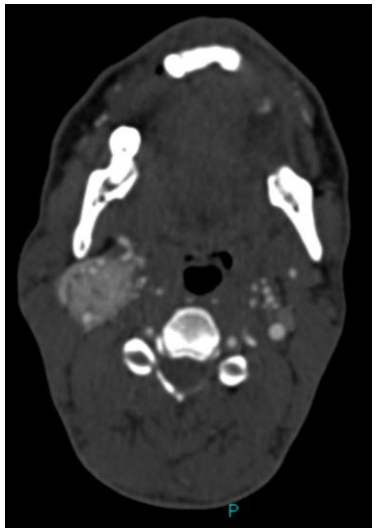
- Establish your team
- Clear responsibilities for members
- Standardise your treatments
- Audit your results
- Don’t dabble











smout71@aol.com