



Localizing studies for primary HPT

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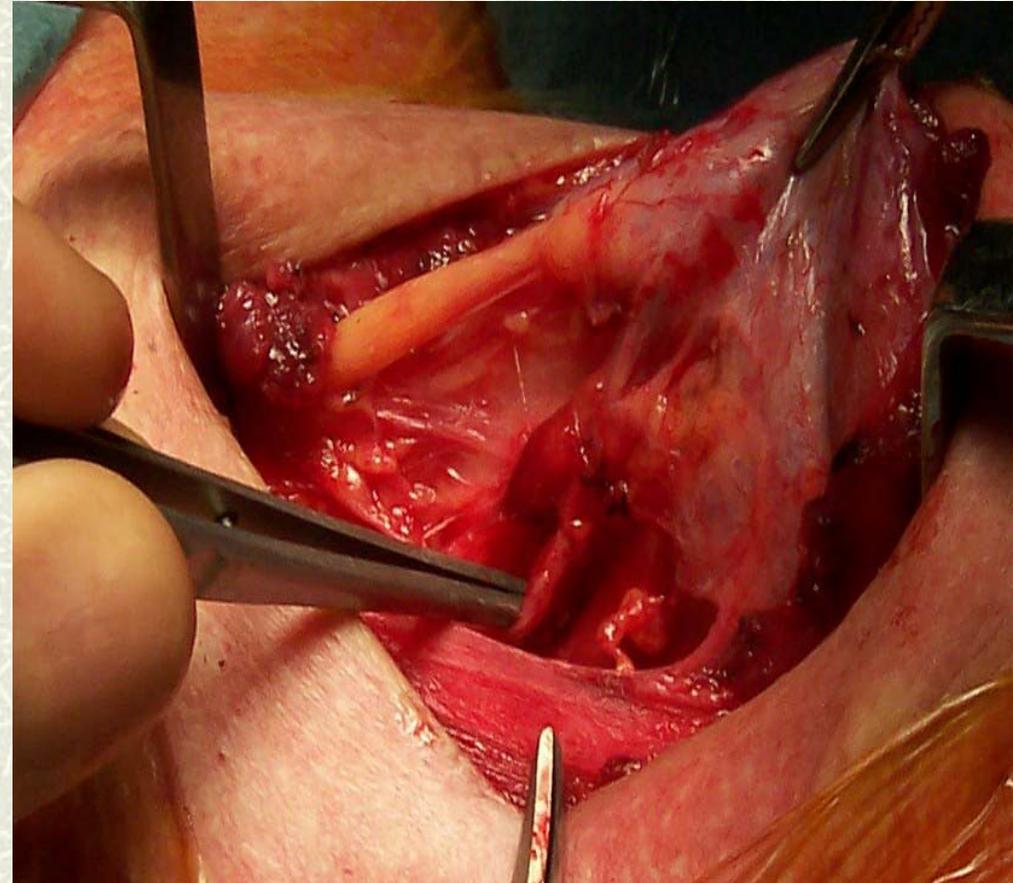
take home message

accurate functional localization is the key to
successful parathyroid surgery in
the minimally invasive era



BNE - the “gold standard”

- # 1- 2 day hospital stay
- # 4 -5 cm cosmetically acceptable incision
- # 98% success rate
- # complication rate < 1%
- # the only localization study required was to localize an experienced endocrine surgeon





the new paradigms for PHPT

multiglandular disease is a common cause of PHPT



most PHPT is due to a single hyperfunctioning gland

4 gland exploration mandatory to ensure high success rate



most patients can be cured by removal of just that single gland

pre-operative localization studies are unnecessary



localization studies essential for focused exploration

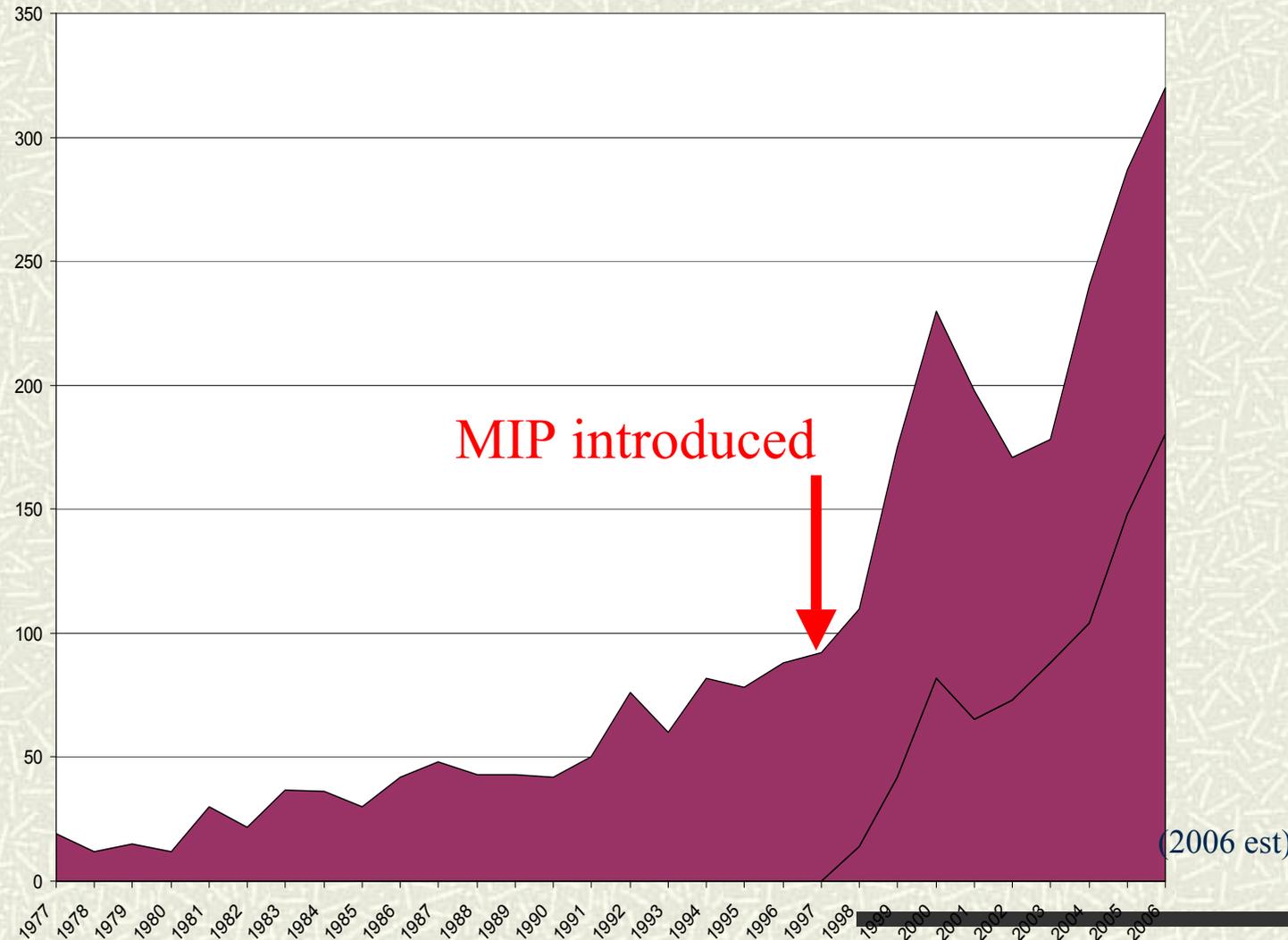
(surgery only indicated for symptomatic disease)

(all patients with PHPT should be offered surgical cure)



University of Sydney data

- parathyroidectomy procedures
- 1977 to 2006
- n = 2741





definition of MIP

- # “focused removal of abnormal parathyroid tissue guided by pre-operative localisation studies and performed through an incision less than 2.5 cm in length”
 - # *Palazzo FF, Delbridge L. Surg Clin NA 2004;84:717-734*
 - # includes the mini-incision focused approach, the video-assisted approach, and cervical endoscopic procedures
 - does not include unilateral exploration via standard collar incision (Russell) or axillary/chest wall endoscopic approaches (Takami)
-



fundamentals of MIP

- # focused removal of an abnormal parathyroid:
 - performed through a small incision
 - guided by localisation studies

MIP = ACCURATE LOCALIZATION

- # all other issues are of marginal relevance
 - use of IO-PTH
 - local *vs* general anaesthesia
 - radioguided surgery
-



MIP is all about accurate localization

- # localization – the ability to delineate the anatomical location of the hypersecreting parathyroid gland causing PHPT with sufficient accuracy to allow a focused surgical approach

 - # FUNCTIONAL – metabolic overactivity = hypersecretion
 - sestamibi scan, or ¹¹C-methionine PET

 - # STRUCTURAL – glandular enlargement = hypersecretion
 - ultrasound, CT, or MRI

 - # COMBINED MODALITY IMAGING – complementary
 - sestamibi CT fusion, or 4D-CT
-



functional localisation studies

- # the breakthrough in preoperative imaging came with the discovery that an agent used for cardiac imaging - Tc99m sestamibi - is avidly taken up by parathyroid tissue, especially adenomas, by virtue of their high mitochondrial content
 - # accuracy rates up to 90%
 - # false positives - hyperplastic thyroid nodules, thyroid cancer, sarcoidosis and lymphomas.
 - # false negatives - 50% associated with multiglandular disease/hyperplasia
-



does technique matter?

Emory data

784 patients with PHPT with 4 different sestamibi imaging modalities compared

planar imaging 77%

multiplanar SPECT 85%

SPECT with thyroid subtraction 68%

SPECT-CT 86%

■ *Sharma J, Mazzaglia P ... Weber C. Surgery 2006 (in press)*



experience is more important

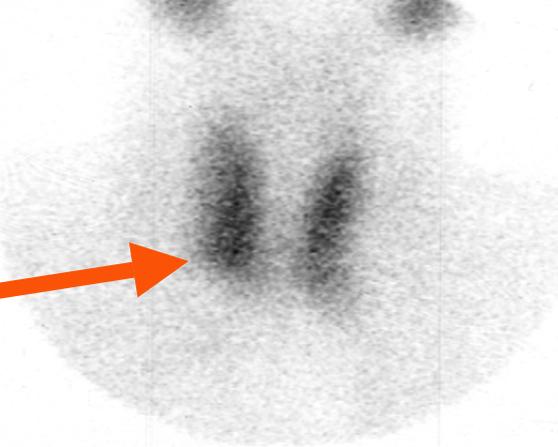


- # planar sestamibi scan (15 mins, 2 hrs)
- # concomitant technetium thyroid scan with oblique views
- # 70% positive of which 94% accurate
 - *Ho Shon I, Bernard E ... Delbridge L. Eur J Nucl Med, 2001; 28:736*



oblique images

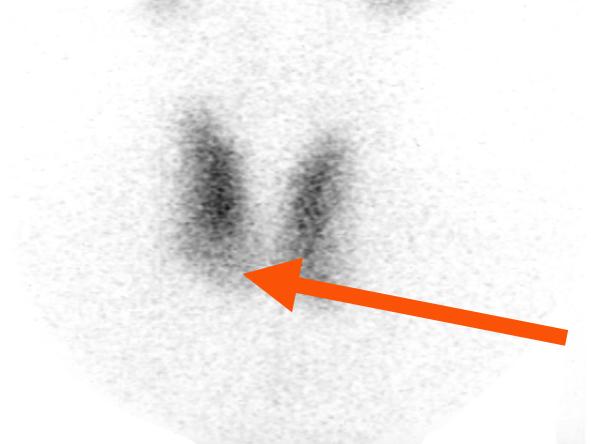
ANT 15 MINS PI



ANT 2 HRS PI



ANT THYROID SCAN



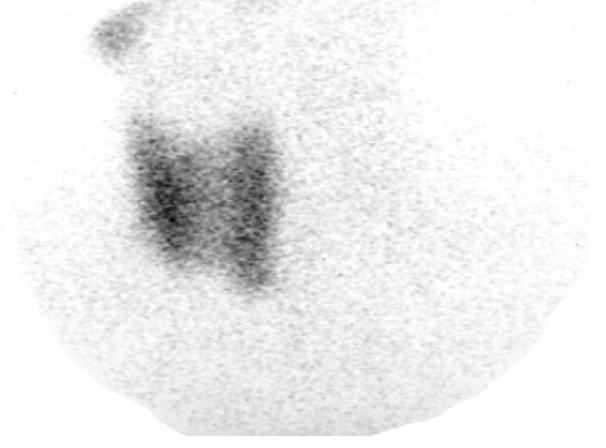
LAO 15 MINS PI



LAO 2 HRS PI



LAO THYROID SCAN





structural localization - ultrasound

- # ultrasound as a localization study is cheap and non-invasive
 - # has been reported to localize between 38% to 93% of parathyroid adenomas
 - # but is clearly operator dependent
 - # not particularly good at localising either ectopic glands or those deep in the tracheo-esophageal groove (descended superior)
-



University of Sydney data

- # 200 consecutive ultrasounds by a single radiologist
 - # correctly predicted surgical findings in 88% of patients.
For single adenomas correlation was 92%
 - *Yeh M, Barraclough BM ... Delbridge L. Endocrin Pract 2006;12:257-63*
 - # surgeon-performed ultrasound equivalent to experienced radiologist
 - # 86% correct prediction of surgical findings
 - # however principally used to guide incision placement
-



surgeon performed ultrasound alone

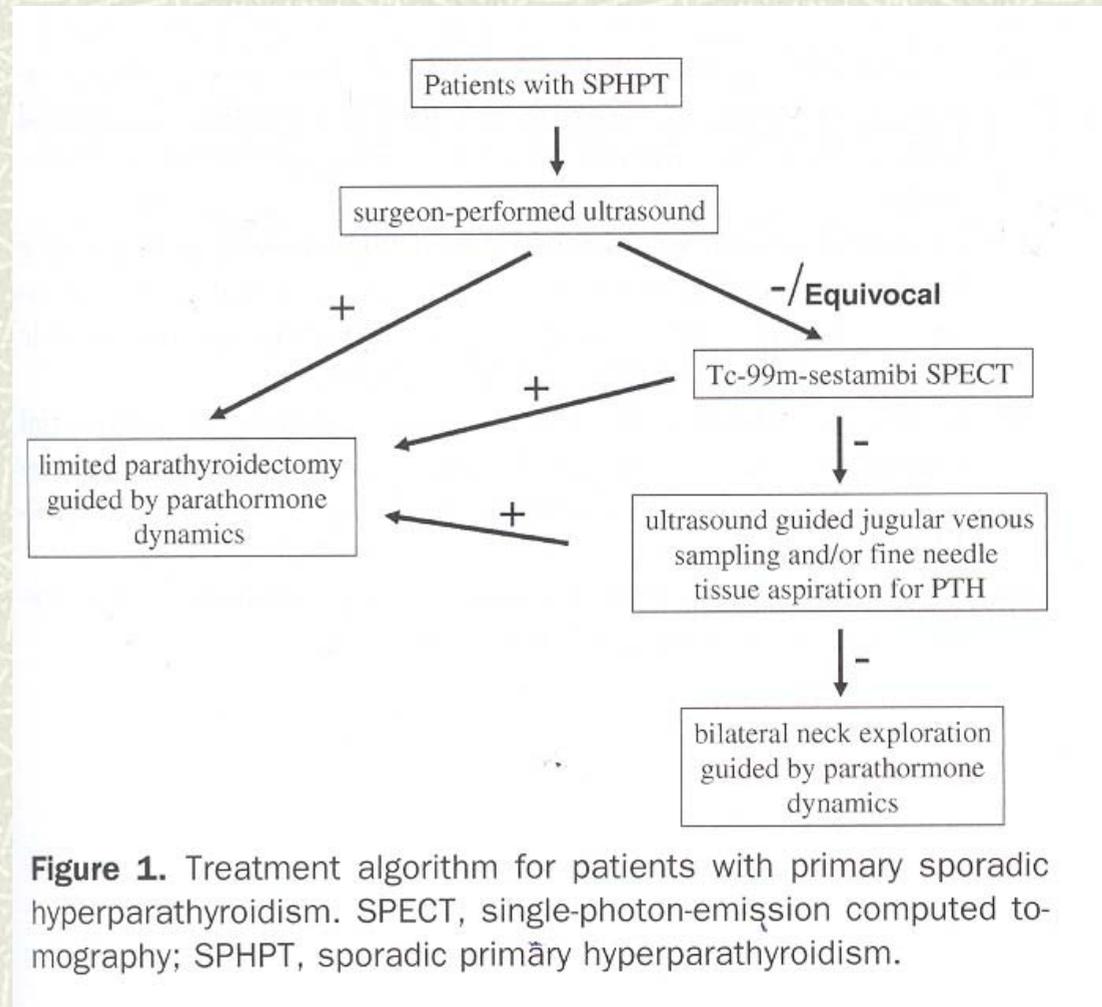
226 patients with PHPT

- surgeon ultrasound (SUS) alone – 173/226 (77%)
- of the remaining 53, sestamibi further identified 30/53 (57%)
- both together identified 90% of glands
- recommend SUS as initial test since less expensive than sestamibi or 3rd party US
- *Solorzano CC, Caneiro D, Irvin GL. J Am Coll Surg 2006;202:18-24*



ultrasound alone

- # surgeon performed US as initial localization
- # sestamibi only if negative or equivocal

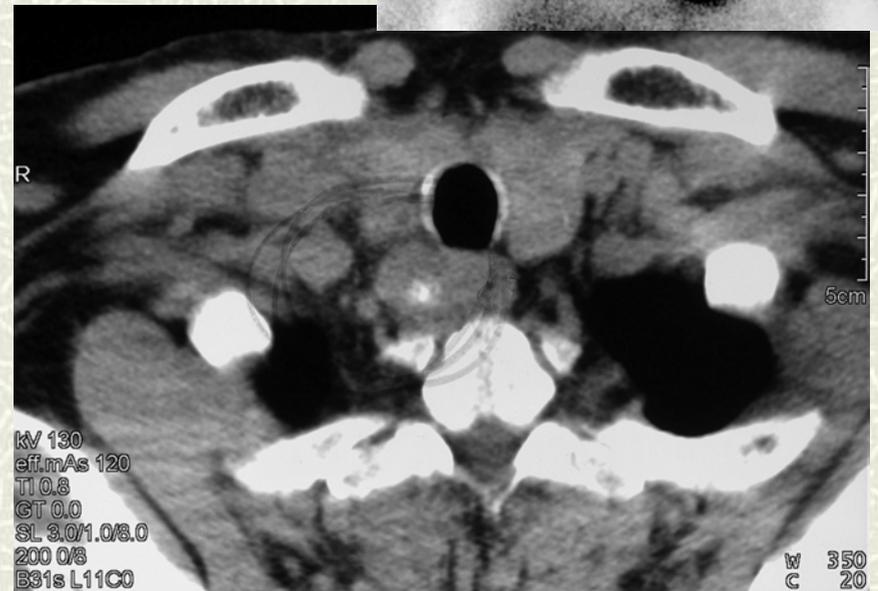
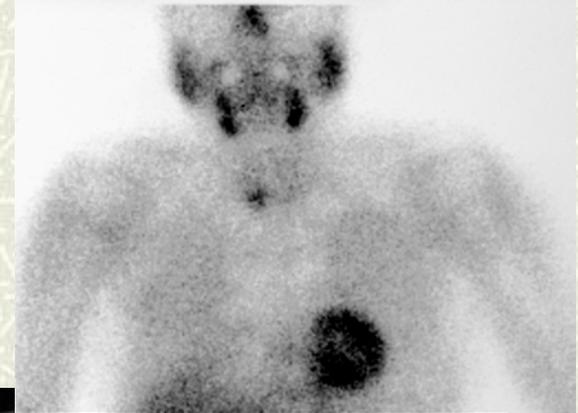




other structural imaging techniques

- # CT and MRI also used with some success particularly in ectopic glands but share similar limitations to US
- # lesions detected on standard CT are either large or potentially malignant.

A CHEST 2 HRS PI





structural imaging issues

- # the principal issue with ultrasound (as with other structural imaging techniques) is that it really only assesses gland size. There are however a number of issues with relying on that alone:
 - “normal” parathyroid glands may be much larger than previously appreciated
 - not all enlarged parathyroid glands are abnormal
 - not all parathyroid adenomas necessarily contribute to the biochemical picture of hyperparathyroidism
-



what is an “abnormal” parathyroid gland

- # the introduction of MIP has been associated with a marked drop worldwide in the reported incidence of multigland disease
- # no change in success rates of surgery

	BNE	MIP
rate of multigland disease	20%	5%
early success rate	98.5%	97.4%

■ *Lee NC, Norton JA. Archives Surgery. 2002;137:896-9*

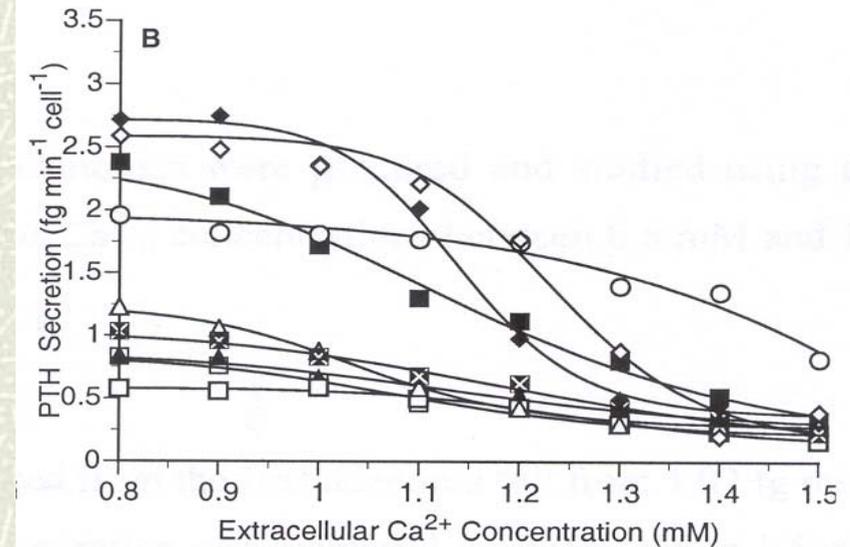
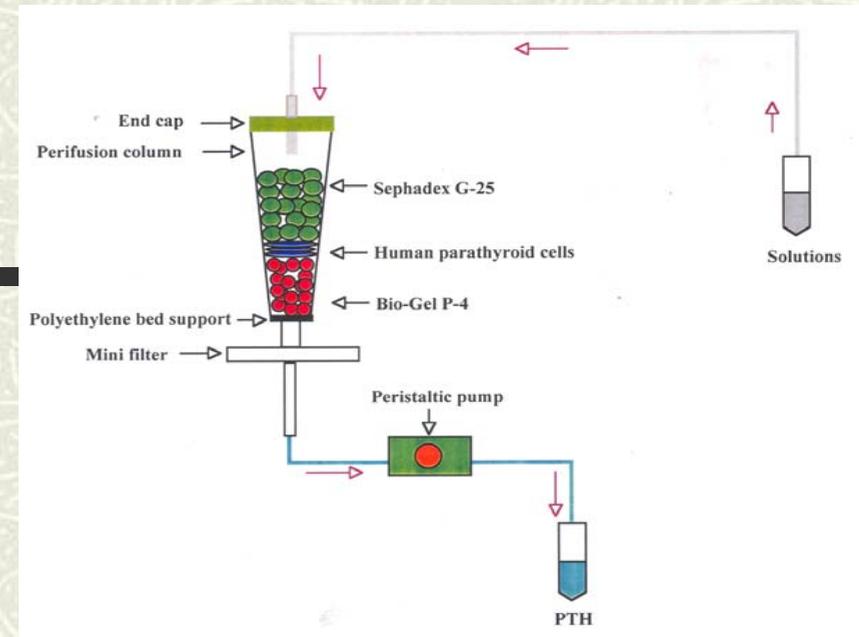
- # some enlarged histologically abnormal parathyroids may not actually contribute to hypercalcaemia = non-functioning adenomas or (parathyroid incidentalomas)
-



■ study of PTH secretory rates in normal and adenomas by perfusion

■ adenomas as a group exhibited considerable heterogeneity with some overlapping normal range

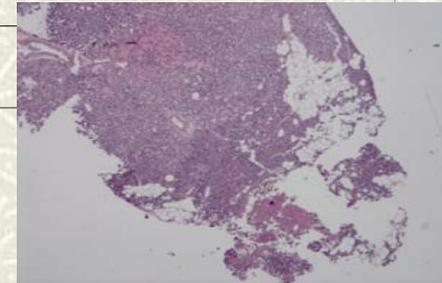
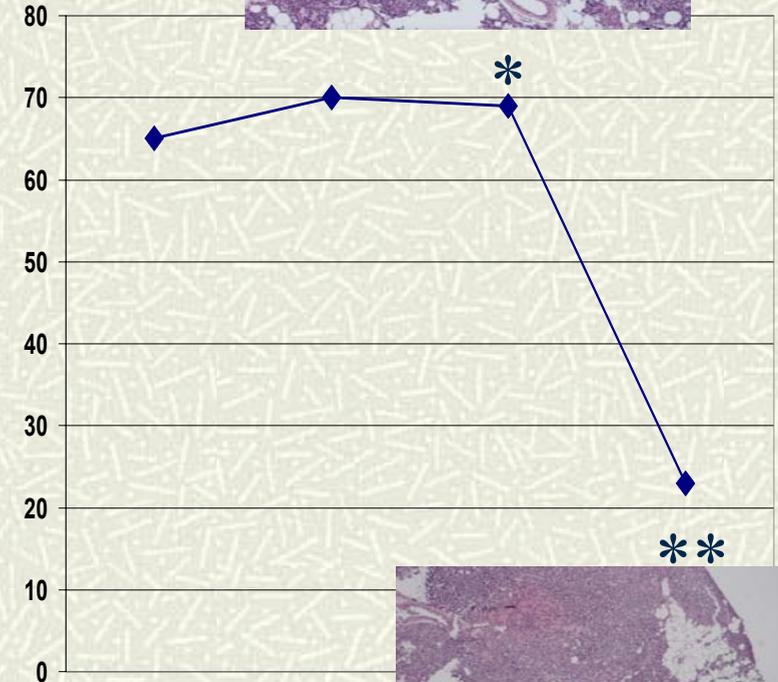
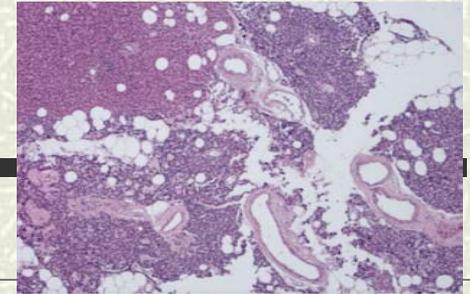
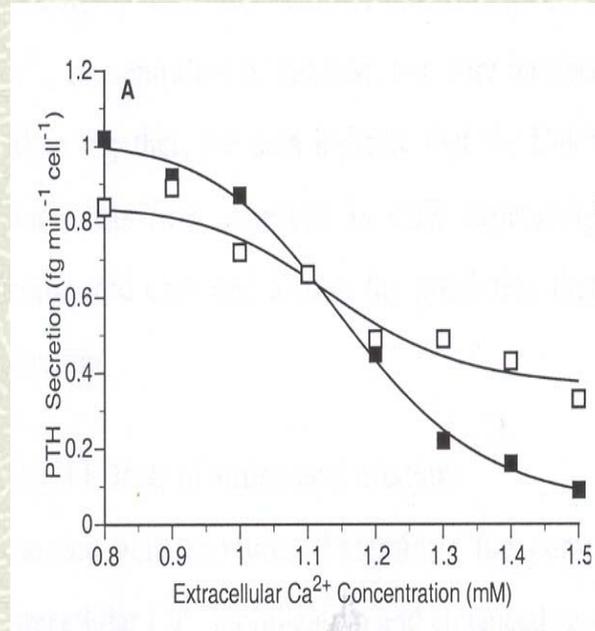
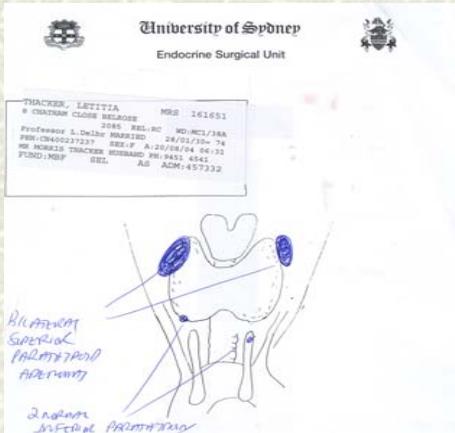
■ *Mun HC, Conigrave A ... Delbridge L. Surgery 2005;138:1111-20*





IO-PTH

- two identical “adenomas removed sequentially at open operation





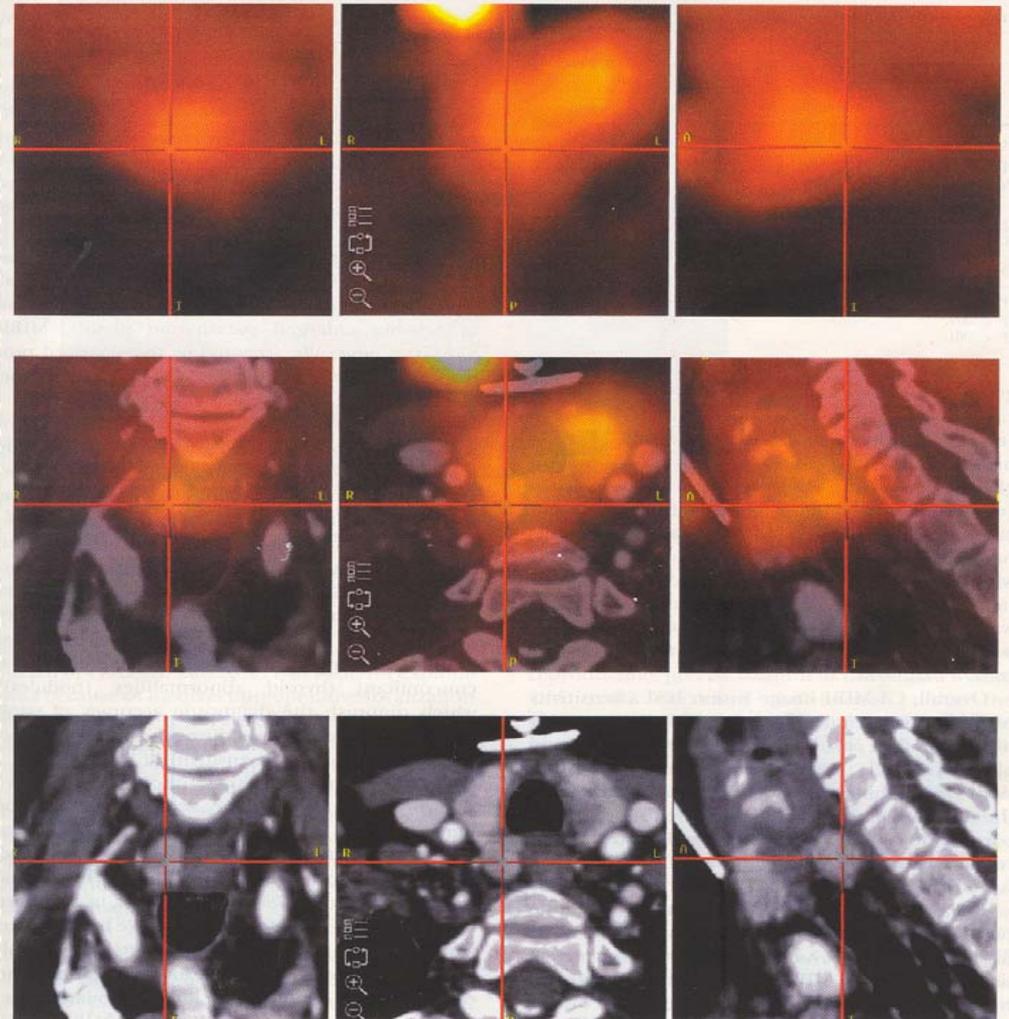
current understanding

- # simplistic view that enlarged parathyroid glands necessarily lead to PHPT is changing
 - # no direct connection between the presence of an adenoma and excess PTH secretion
 - # there may well be a whole spectrum of function associated with parathyroid adenoma
 - cf adrenal incidentaloma
 - eg incidental enlarged parathyroids at thyroidectomy (2%)
-



combined modality localization

- # CT-MIBI image fusion techniques
 - 24 consecutive pts
 - sensitivity 93%
 - specificity 100%
 - increase percentage of patients suitable for MIP
- *Profanter et al 2004. Surgery 135:157*





4D-CT scan

4D-CT is basically a CT angiogram which uses flow as a surrogate for function

- *Rodger SE, Doherty D ... Perrier N. Surgery 2006 (in press)*





3-D reconstruction of 4D-CT





3-D reconstruction of 4D-CT





results

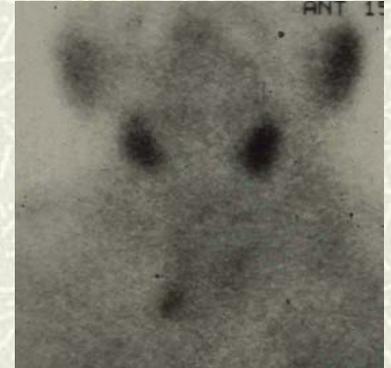
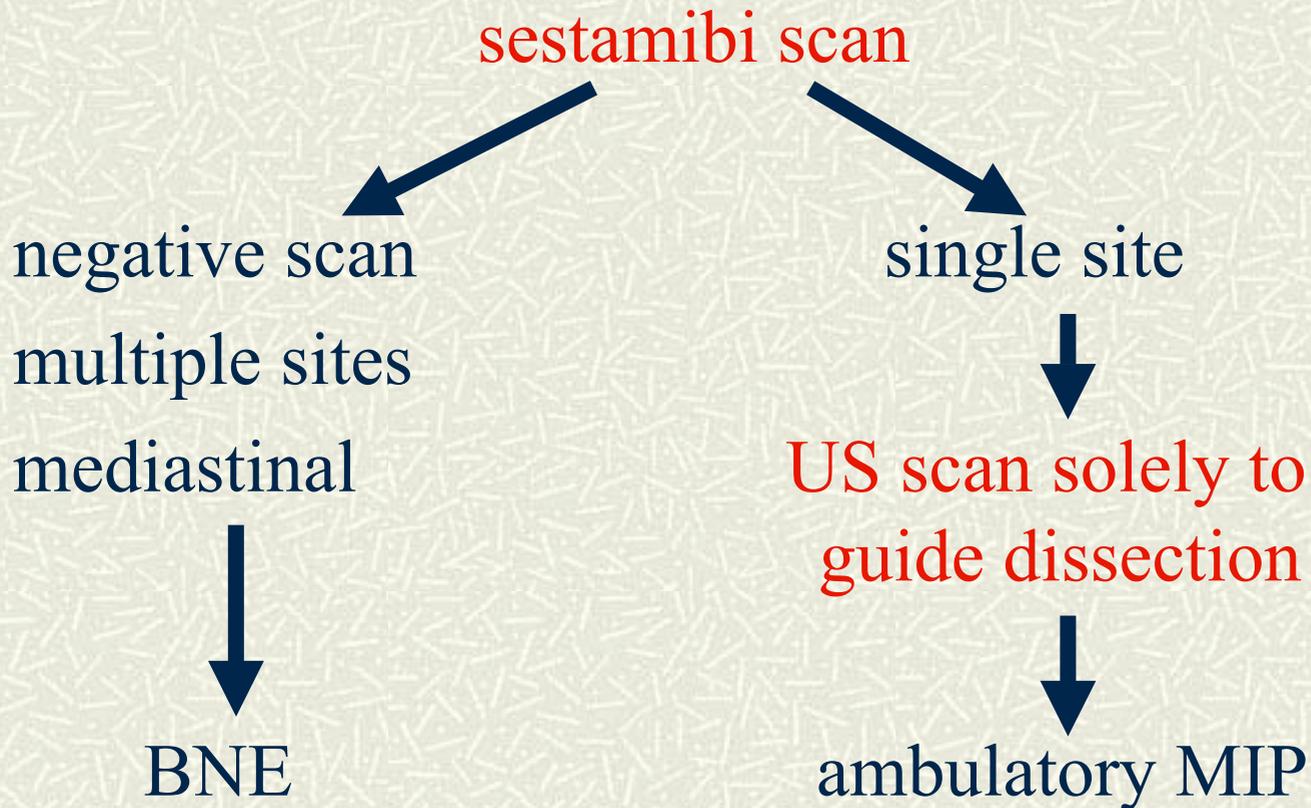
- # 75 patients having sestamibi, US and 4D-CT compared to operative findings (localization of hyperfunctioning parathyroid glands to the correct quadrant of the neck)

	sensitivity	specificity
■ 4D-CT **	70%	89% (**p<0.0006)
■ Sestamibi	33%	83%
■ US	29%	86%

■ *Rodger SE, Doherty D ... Perrier ND. Surgery 2006: in press*



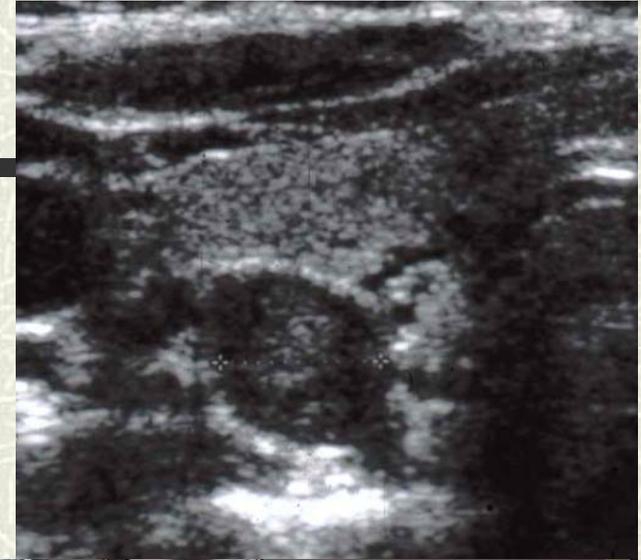
University of Sydney protocol





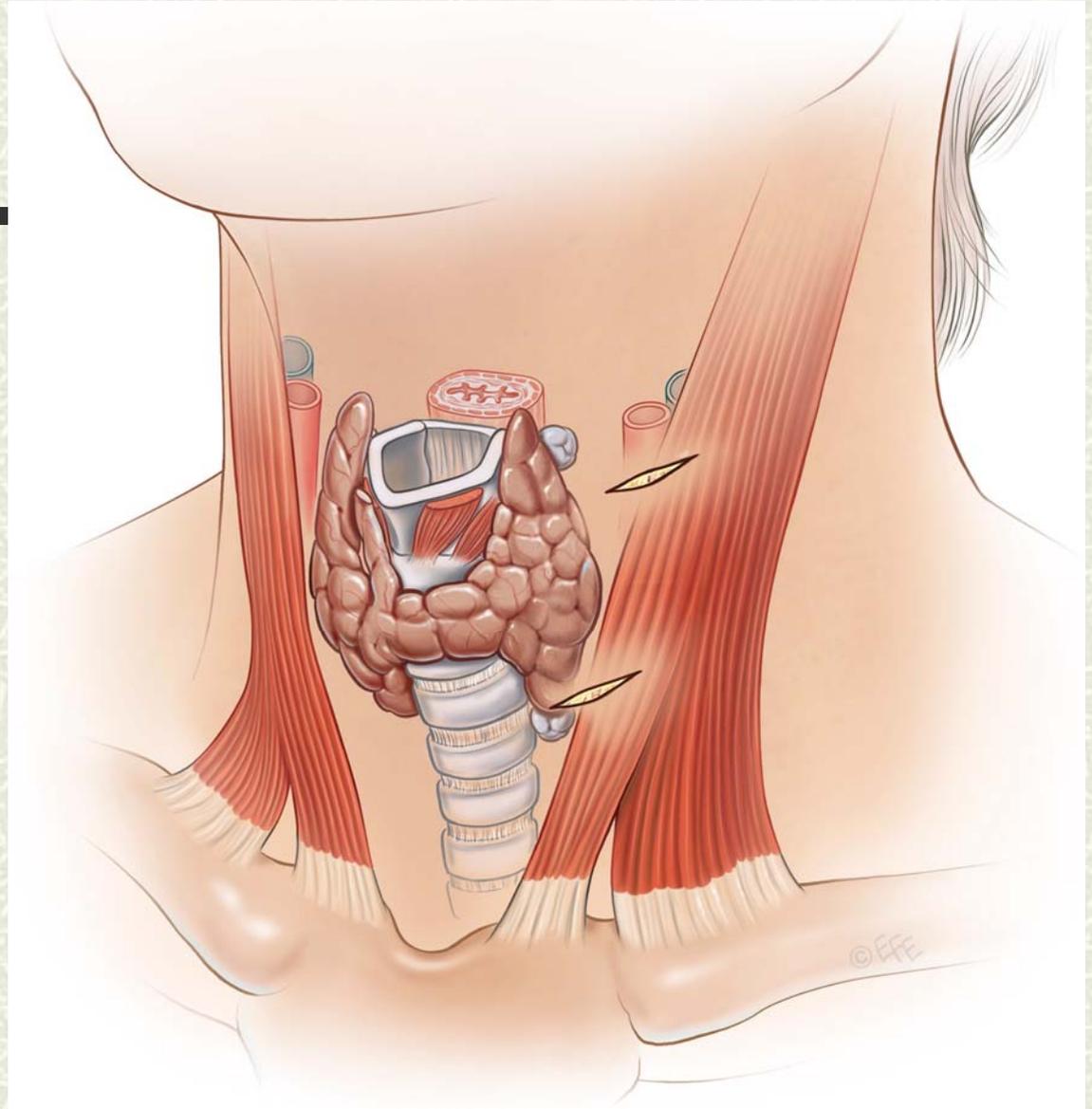
role of ultrasound

- # subsequent ultrasound of the site identified by sestamibi scan provides the anatomical details necessary for localization-based focused surgery
- # surgeon performed ultrasound in the operating theatre more accurate and more relevant





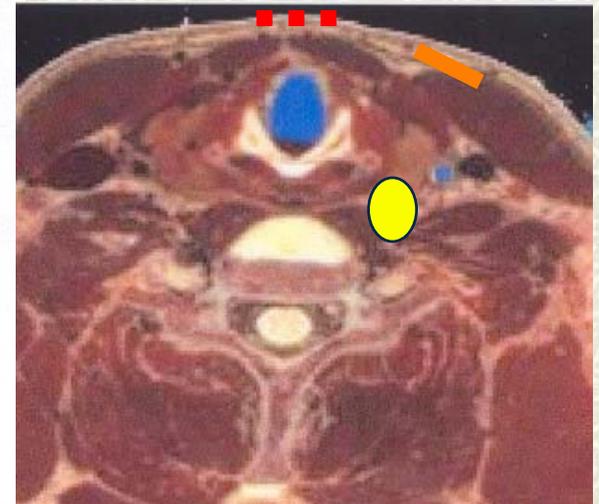
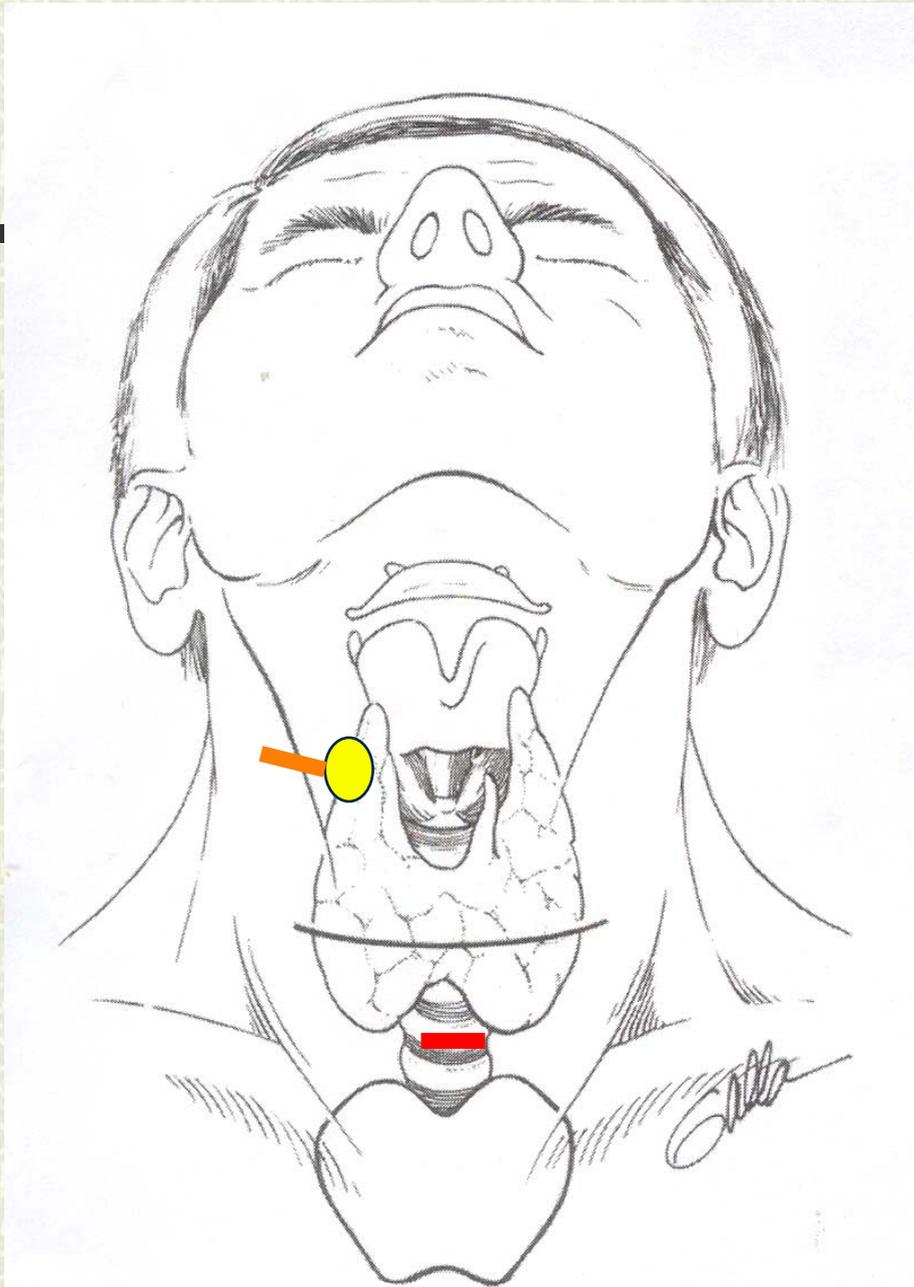
- # localization based MIP
- # just place a small incision directly over the adenoma and take it out!





superiorly
located
adenomas

- true superior
(posterior, often
above Tubercle
of Zuckerkandl
or behind upper
pole)





technique of localization based MIP



2 cm lateral incision
overlying site of
localized adenoma





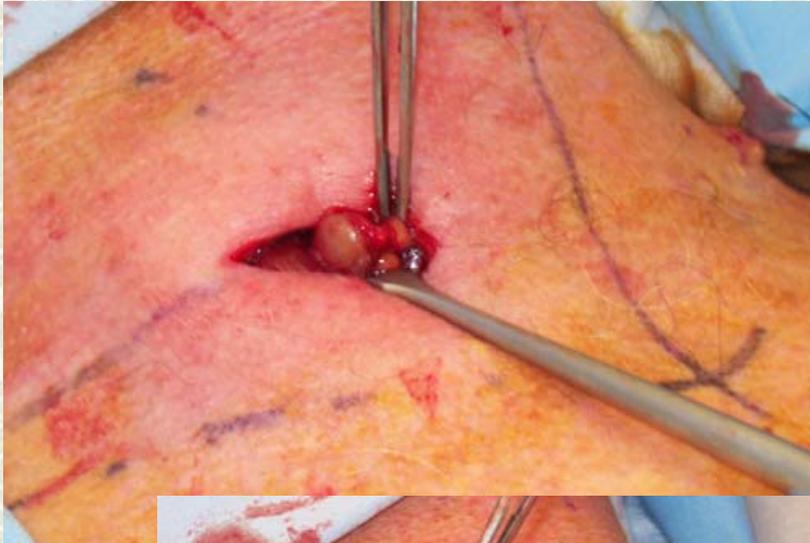
working space

working space
created with finger
dissection through
2cm incision and
tumor removed
under direct vision





removal and closure



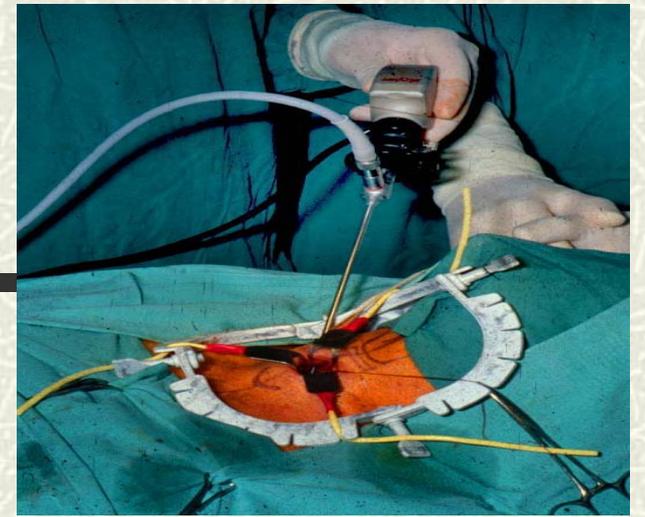
direct removal of
adenoma





what about adjuncts?

- # endoscopic surgical technique
- # intra-operative nuclear probe as guide to dissection
- # IOPTH
 - do any of these techniques improve the outcomes compared to localization based MIP?





does IOPTH add to localization-based MIP?

- # 100 consecutive patients with single site of uptake undergoing MIP
- # IOPTH data collected but not acted upon
- # analysed subsequently by Miami criteria
- # 98% cured regardless
- # IOPTH would have cured only one more patient
- # “value-added” accuracy of IOPTH is only 1%
 - *Stalberg P, Sidhu S ... Delbridge L. J Am Coll Surg 2006;203:1-6*



“value-added accuracy” = 1%

<i>scan based</i>	cured by MIP	98
100	failed first op	2*
	unnecessary conversions	0
+ <i>IOPTH</i>	cured by MIP	90
100	cured by conversion	9
	failed first op	1*

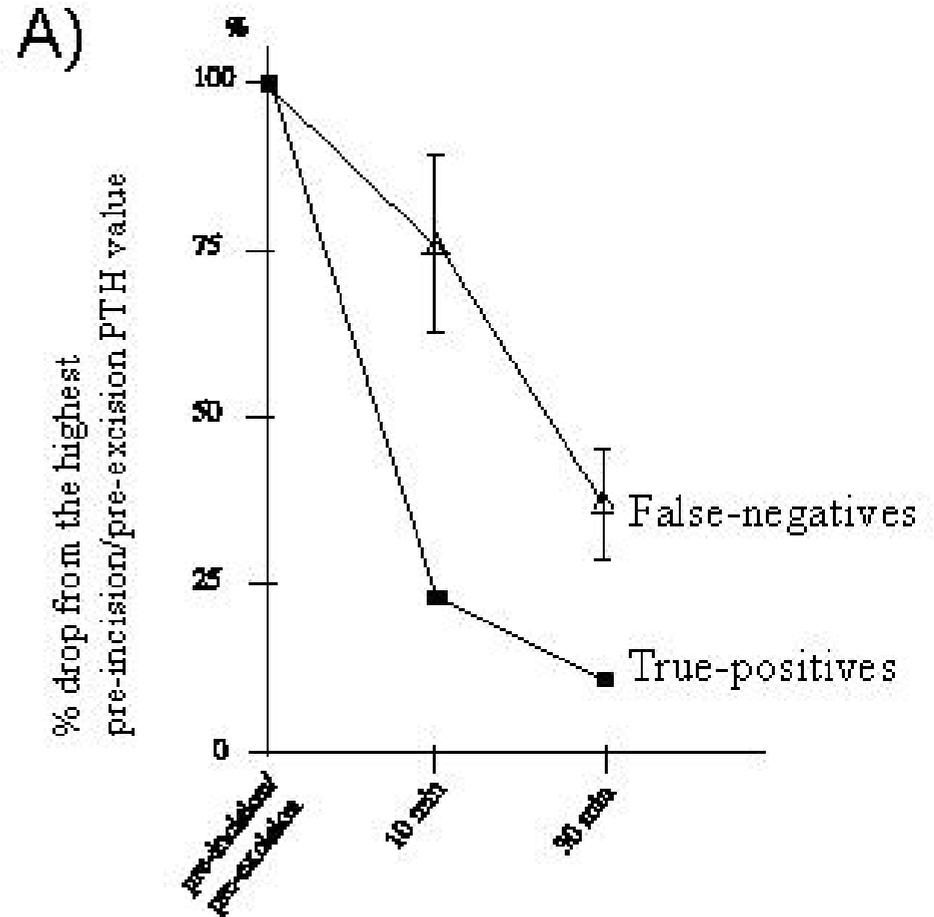
* all patients fully informed of 2% need for re-operation



IOPTH and false negatives

false negatives

- 10 minutes – 9% unnecessary conversions
- 30 mins – 4% unnecessary conversions but with added OR time





scoring systems to fine tune decision

- # CaPTHUS score = Ca (>12mg/dL) + PTH (>2Xnormal)+ concordant ultrasound/sestamibi
- # if greater than 3 has a 100% positive predictive value for single gland disease
- # allows localized based MIP without any adjuncts
- # less than 3 requires a “different approach”
 - *Kebebew E, Hwang J ... Clark O. Arch Surg 2006;141:777-82*



negative localization

- # what to do if sestamibi is non-contributory
 - OPTION 1: rely on another localization modality eg ultrasound
 - still an effective strategy but with some risk
 - OPTION 2: MIP with intra-operative adjuncts
 - uncertain localization magnifies potential flaws
 - OPTION 3: repeat sestamibi after time lag
 - OPTION 4: offer open BNE
-



repeat sestamibi

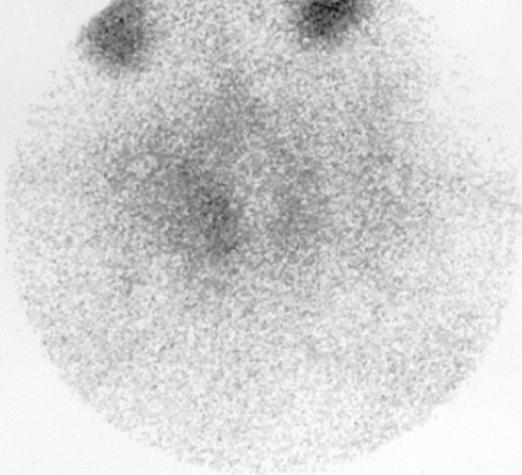
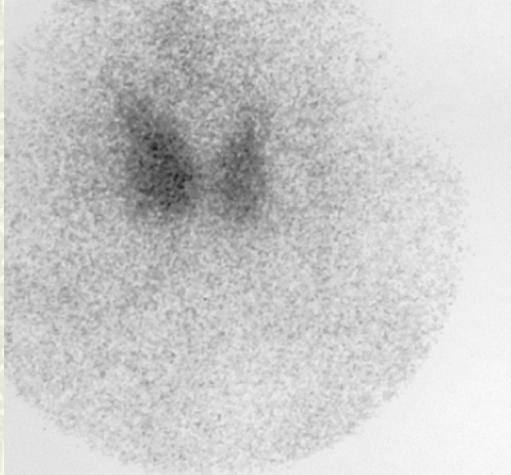
- # gland function and secretion may be variable
 - # repeating sestamibi scan after a set period may be valuable (especially if initial scan done in peripheral or inexperienced centre)
 - # important to do high quality scan 2nd around
-



repeat imaging

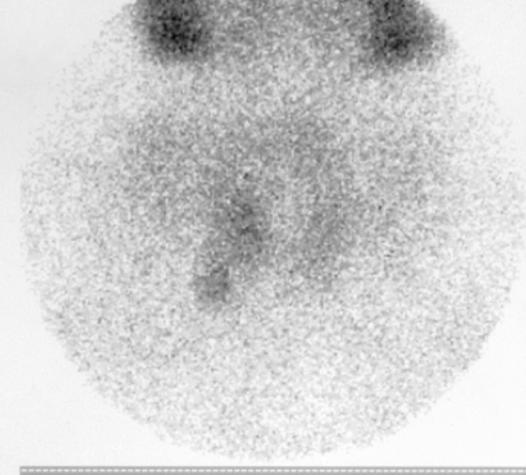
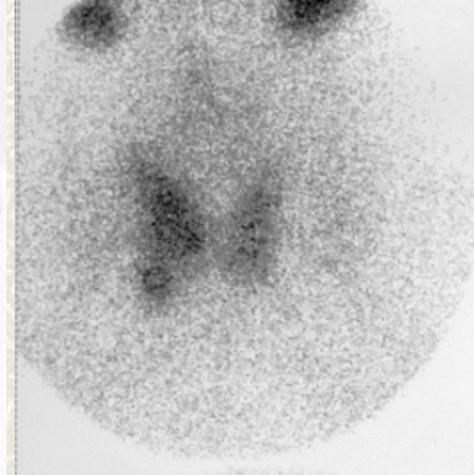
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ANT 2 HRS PI

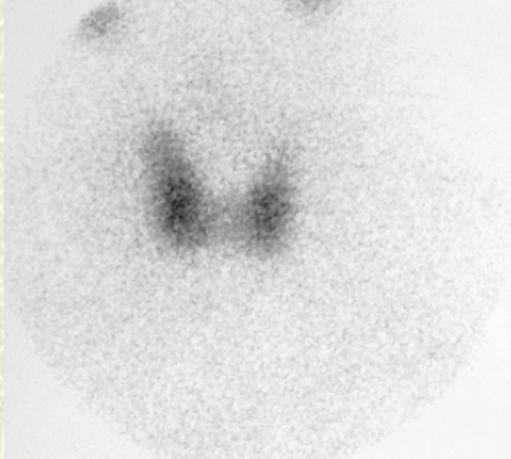


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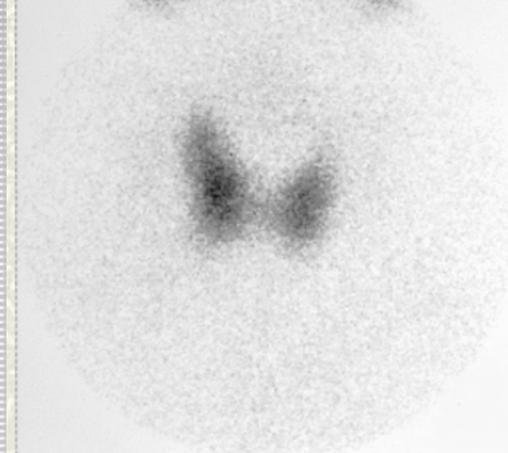


ANT THYROID SCAN



initial scan

ANT THYROID SCAN



6 mths later



offer open procedure

- # negative imaging studies are inevitable in the overall population of patients with PHPT
- # related to MGD/hyperplasia
- # also related to histological characteristics of the tumour
- # negative scan - chief cell predominance (26/36) positive scan – oxyphil cell predominance (21/32)
 - *Mihai R, Gleeson F ... Sadler GP. World J Surg 2006;30:697-704*



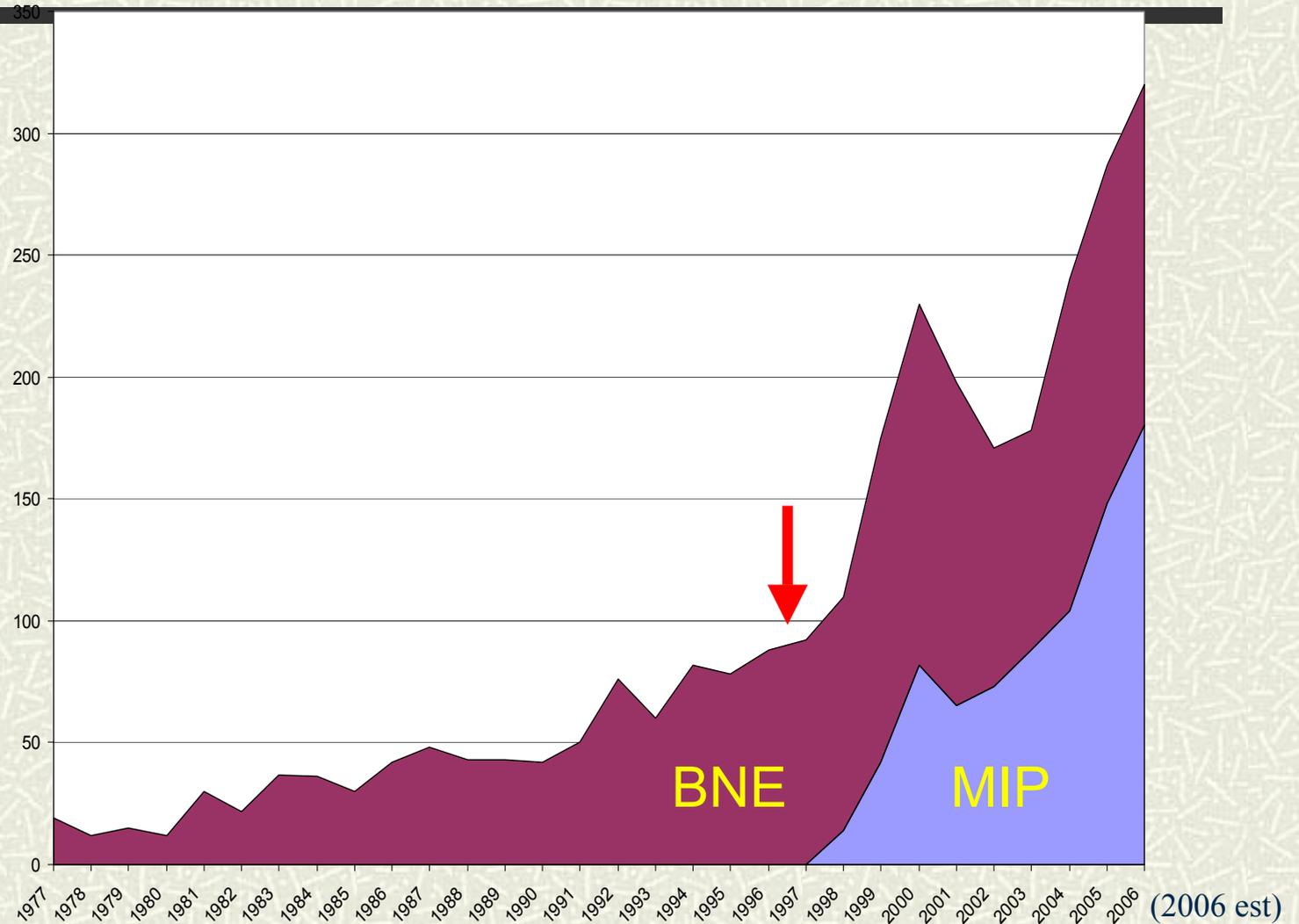
University of Sydney data

parathyroidectomy
1977 to 2006

MIP introduced
1998

numbers increased
30 cases per year to
over 300 per year

just over 60% of
increase only due to
MIP





perception of parathyroid surgery!



“ a recommendation for an invasive procedure is not always met with ready acceptance”

■ *Bilezikian 2001*



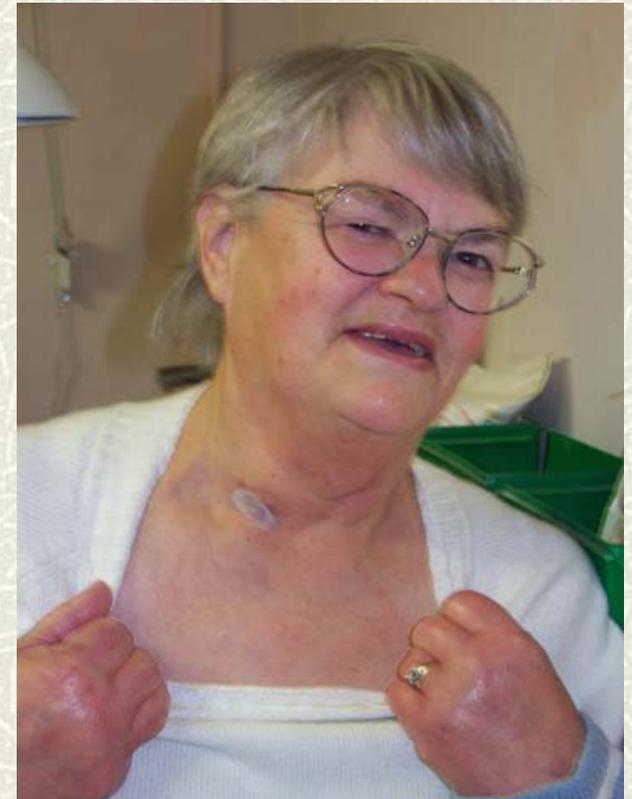
“ a parathyroidectomy nowadays seems to have about as much impact on the patient as having a skin lesion removed”

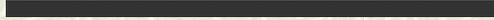
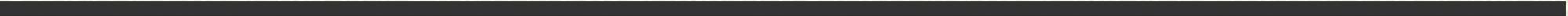
■ *Posen 2006*



take home message

- # accurate functional localization is the key to successful parathyroid surgery in the minimally invasive era
- # it allows an ambulatory mini-incision procedure, without the need for adjuncts, with a 98% success rate, in 60-70% of patients with PHPT







what about ectopic localization?

- # commonest site is intrathymic in anterior mediastinum
- # cervical thymectomy routinely performed as part of BNE
- # what about cervical thymectomy during MIP?



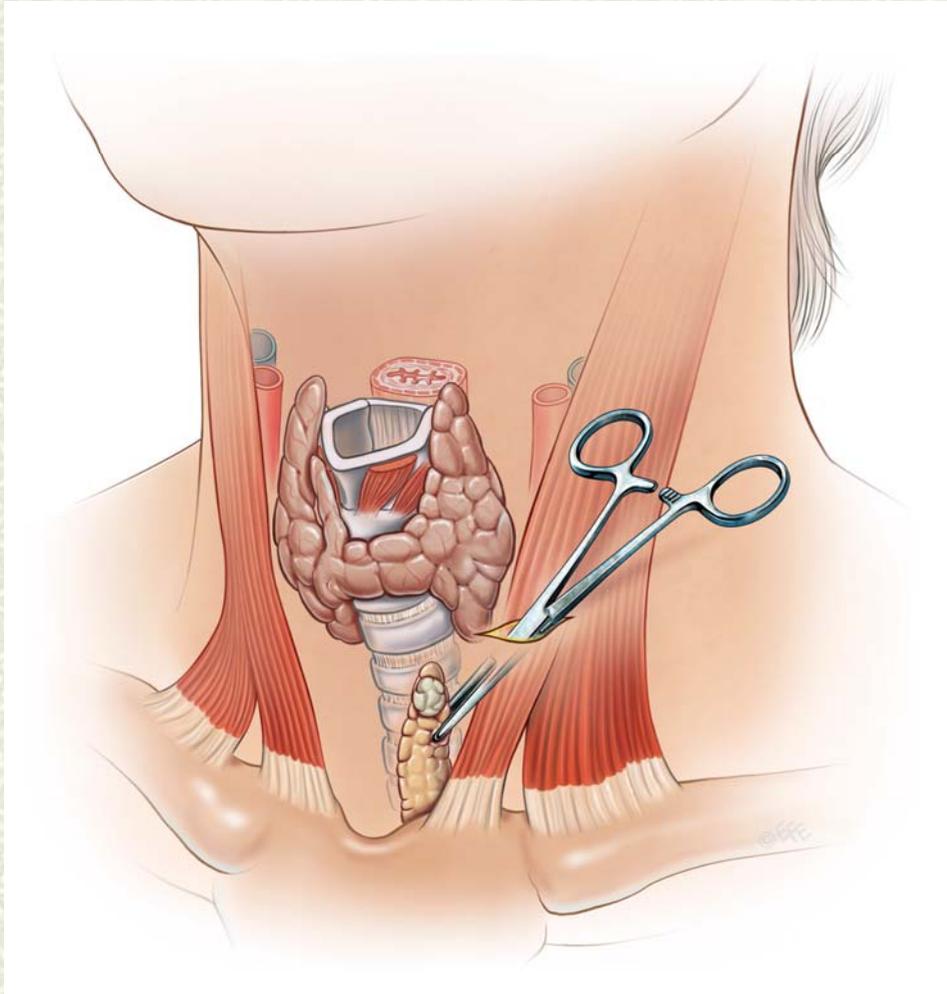


University of Sydney experience

- 5 years to Dec 2005 – 144 patients having thymectomy during surgery for primary HPT
 - 99 via initial BNE
 - 4 requiring sternotomy
 - 15 via MIP converted to open
 - 30 via MIP
 - mean 34 mm (8-85mm) thymic tissue removed
 - 5 (16%) fibrofatty/lymph nodes tissue only
 - 1 neuropraxia/no other complications
 - *Stalberg P, Grodski S, ..., Delbridge L. Surgery 2006 (submitted)*
-



cervical thymectomy during MIP



- # thymic tissue grasped with hemostat
- # gentle traction allows thymus (and intrathymic parathyroid adenoma) to be removed