



**Annual Meeting
October 21st & 22nd 2010**

**Austin Court
Birmingham**

Abstracts For Presentation

Free Papers Session 1

Friday 22nd November 8.45am to 10.15am

Chairs

Mr Barney Harrison

Ms Helen Doran

Time Allocated per paper: 10mins

Safety and Efficacy of Minimally-Invasive Parathyroidectomy (MIP) under Local Anaesthesia.

Michael J Stechman, Rajeev Parameswaran, Hilary Bridge, Radu Mihai, Gregory P Sadler.

Department of Endocrine Surgery, John Radcliffe Hospital, Headington, Oxford, UK.

Background. Patients with primary hyperparathyroidism (PHPT) and concordant ⁹⁹Tc-sestamibi and neck ultrasound are suitable for MIP. This prospective study aimed to determine the safety and efficacy of MIP under local anaesthesia (LA), without intra-operative PTH (io-PTH) measurement.

Methods. A prospective database was used to collect data on consecutive patients undergoing MIP via the lateral mini-incision approach. The technique involved LA (bilateral superficial cervical plexus blocks with 0.25% bupivacaine) and sedation (intravenous remifentanyl/propofol) without io-PTH. No patients were excluded based on age or anaesthetic risks. Data on operative time, conversions to bilateral neck exploration, length of stay, post-operative normocalcaemia and complications were collected prospectively.

Results. Fifty-six patients (44 Female; median 64 years) had day case MIP under LA. Mean pre-operative serum calcium and PTH were 2.78 ± 0.18 mmol/L and 17.3 ± 14.7 pmol/L, respectively. The mean operative-time was 38 minutes, one patient required conversion to bilateral neck exploration (false-positive localisation of a papillary thyroid microcancer) and one required extension of the mini-incision for intra-operative bleeding. All patients but one were discharged less than 6 hours post-operatively. At a median of 2 months follow-up, fifty-five patients were normocalcaemic (mean $Ca^{++} = 2.34 \pm 0.13$ mmol/L, 98.2% cure). There were no recurrent laryngeal nerve injuries, episodes of post-operative bleeding or unplanned readmissions.

Conclusions. MIP under LA and sedation without io-PTH is a safe and effective treatment for pHPT with the added benefit of same day discharge in nearly all patients. The technique has a similar complication profile to MIP under GA and makes ambulant surgery feasible including in those not fit for GA.

THYROID HURTHLE CELL CARCINOMA: A TERTIARY INSTITUTION EXPERIENCE

Paunovic I, Diklic A, Zivaljevic V.

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AIM OF THE STUDY

Hurthle cell tumors (HCT) comprise 3-10% of all epithelial thyroid tumors. Discrimination of Hurthle cell carcinoma (HCC) from benign Hurthle cell tumors (HCA), typology of HCC and choice of optimal treatment continue to be open issues in thyroid surgery.

The objective of the study was to report a series of patients with HCT with a special accent on HCC.

MATERIAL AND METHODS

The study is based on review of medical records of 199 patients diagnosed with HCT who underwent thyroid surgery at the CES between January 1982 and December 2002. Data were analyzed retrospectively and prospectively.

RESULTS

88 patients(44%) presented with HCC. HCC patients were 48 years of mean age, average duration of the disease was 6 years, 85% female, 66(75%) with solitary and 22(25%) with multinodular goiter. 2 patients were hyperthyroid. The average size of tumor was 4.8 cm(range, 1.0-15.0 cm). Positive lymph nodules at surgery were confirmed in 4(4.5%), distant metastases were not verified. The majority of the patients were in T2(44) and T3(35) group. Total thyroidectomy was performed in 87.5% patients. Duration of follow up for 76(87%) patients was from 1 month to 216 months(18 years) with average duration of 79 months(6.5 years). The follow up for 29(38%) patients was less than 5 years and for 47(62%) more than 5 years. Local recurrence was found in 4(5%) patients(range of duration 1-7 years, average 3.7 years). Temporary laryngeal nerve palsy and temporary hypoparathyroidism were confirmed in 2(2.27%) and 3(3.41%) patients respectively.

CONCLUSION

There was no difference between HCA and HCC linked to patient age. Duration of the disease was significantly longer in patients with HCC. HCT size is predictive of malignancy. The majority of HCC was graded T2 and T3 stadium and stage II disease. HCC is rather uncommon, therefore there is no first class hands-on experience at any single institution.

Definition and Outcome of Massive Adrenal Tumours

James Kirkby-Bott FRCS (Gen.Surg),
Melwyn Sequeira MD,
Ziad El-Khatib MD,
Robert Caiazzo PhD,
Sebastien Aubert PhD,
Emmanuelle Leteurtre PhD,
Laurent Arnalsteen MD,
Francois Pattou PhD,
Bruno Carnaille MD

CHU Lille, France

Background

This series aims to define what constitutes an abnormally large adrenal tumour, what pathologies cause these tumours and what the outcome is.

Method

Between 1992 and 2009 we searched the adrenal database for cases that fell between the 95th and 100th percentile range for size. The measurement taken post-excision was used to determine the size of the tumour

Results

Fifteen centimetres (cm) was the definition of a massive adrenal neoplasm as this was the size to the nearest cm that straddled the 95th percentile. 33 patients were included in the analysis. 14 tumours were hormone secreting. Median tumour size was 17 cm (range 15 to 30). 24 patients had malignant tumours. Pathology included: 20 adreno-cortical carcinomas, 5 pheochromocytomas, 2 adrenal metastases, 2 adrenal sarcomas, 2 necrotic adrenal glands and one each of: schwannoma and myelolipoma. An R0 resection was accomplished in 22 patients. Five of 20 patients with adreno-cortical cancer are disease free, 6 have recurred and 9 have died. 5/24 patients with cancer presented with an inferior vena cava (IVC) tumour thrombus (median survival 5.5 months. Median survival was 13 months for cortico-adrenal cancers. Kruskal-Wallis shows no difference in overall follow-up. Mantel-Cox regression is also not significant.

Conclusion

A massive adrenal neoplasm is an adrenal tumour greater than 15cm. Malignant cortico-adrenal cancers are the commonest encountered massive adrenal neoplasm. All patients with a massive adrenal neoplasm should be operated on because 25% are benign and some cancers can be cured. Patients with IVC tumour thrombus should be discussed.

Robotic-Assisted Parathyroidectomy: A Feasibility Study

Neil Tolley¹, Asit Arora¹, Fausto Palazzo¹, George Garas¹, Ranju Dhawan², Jeremy Cox¹, Ara Darzi³

1. Department of Endocrine and Thyroid Surgery, Imperial College Healthcare NHS Trust, London
2. Department of Radiology, St Mary's Hospital, Imperial College Healthcare NHS Trust, London
3. Department of Biosurgery and Surgical Technology, St Mary's Hospital, Imperial College London

Background: Targeted parathyroidectomy is the gold standard approach for localised parathyroid disease. However, a robotic assisted approach has not been investigated. The aim was to assess the feasibility of a robotic-assisted technique which avoids a neck scar.

Method Ten patients underwent robotic assisted parathyroidectomy (RAP) for primary hyperparathyroidism. Outcome variables assessed were operative time, voice change, biochemical cure and histopathological confirmation.

Patient-reported outcome measures (PROMs) included subjective assessment of pain and scar cosmesis, Voice Disability Index 2 and EQ-5D quality of life assessment. Mean length of follow up was 5.4 months.

Results The parathyroid adenoma was successfully removed in all cases with negligible blood loss and 1 RAP conversion. Subjective voice assessment demonstrated no evidence of voice change in all cases. Robot docking and exposure times plateaued to 20 minutes after 2 and 4 cases respectively. The mean robot operative time (55 minutes) was affected by body habitus and size of the lesion. The mean VAS for scar cosmesis was 71% on the first day and improved to 91% at 6 months. Pain decreased to 9% at 2 weeks. The 5 EQ-5D quality of life parameters all significantly improved following targeted robotic surgery.

Conclusion. This pilot study demonstrates that the RAP technique is feasible, offers a high cure rate with minimal postoperative pain, short hospital stay, a rapid return to daily activities and excellent patient satisfaction. It represents a viable alternative to existing targeted approaches and offers the additional advantage of no scar in the neck.

The Birmingham Protocol: Identifying and Managing Post-Thyroidectomy Hypocalcaemia: An Update

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Abstract: Temporary hypocalcaemia following total thyroidectomy occurs in around 30% of patients. Common practice dictates a post-surgery protocol to allow the early identification of this complication, more of which are utilising parathyroid hormone (PTH) assays. Unfortunately there is no widely accepted national protocol which incorporates the test, despite the growing body of evidence supporting its use.

To address this, we have previously presented an evidence-based protocol for the identification and management of post-thyroidectomy hypocalcaemia, which has the advantage over other protocols in that it allows for the lack of out-of-hours PTH assay availability in many hospitals without compromising patient safety. We propose that it is possible to accurately identify patients who will not suffer hypoparathyroidism, allowing their safe and early discharge. We have tested the protocol on 40 consecutive patients undergoing total/completion thyroidectomy. No patients would have been discharged to subsequently develop hypocalcaemia. One patient was identified as at risk (low PTH and borderline calcium) and went on to become hypocalcaemic. 11 patients became hypocalcaemic, 6 had normal PTH and the calcium normalised by Day 2. Five had low PTH, which normalised in 4 but remained low in 1. All of these patients would have been identified and treated appropriately by the protocol. No patients with PTH>20pmol/L and calcium>2.1mmol/L developed hypocalcaemia.

We propose that this protocol could be adopted nationally and may be of use in centres wishing to undertake day-case thyroidectomy.

References:

Cooper MS, Gittoes NJ. Diagnosis and management of hypocalcaemia. *BMJ*. 2008;336(7656):p1298-302.
Sharma N, et al, BAETS Meeting 2008
Sharma N, et al, *Endocrine Abstracts*. 2010;21:p395

Can postoperative hypocalcaemia be predicted in patients undergoing parathyroid surgery?

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Background

Hypocalcaemia following surgery for primary hyperparathyroidism is common, but difficult to predict. The need to monitor postoperative calcium levels may prolong hospital stay. We undertook a retrospective study of preoperative indices in an attempt to identify risk factors for the development of postoperative hypocalcaemia.

Methods

Patients undergoing surgery between January 2005 and May 2010 for primary hyperparathyroidism were identified using hospital coding data. Preoperative parathyroid hormone (PTH) and pre- and postoperative corrected calcium (cCa) were collected. Pathology was reviewed. Statistical analysis was performed using Chi-squared test and logistic regression.

Results

Two hundred and sixteen patients were identified. Three were excluded due to incomplete data. Histology showed single adenoma, hyperplasia, double adenoma and normal parathyroid tissue in 81.7%, 16%, 1.4% and 0.9% respectively.

Hypocalcaemia (cCa <2.10mmol/l) occurred in 25.8% of patients within the first three postoperative days. Patients who developed hypocalcaemia had a significantly lower mean preoperative calcium than those who were normocalcaemic postoperatively (2.67mmol/l vs 2.77mmol/l, $p=0.001$).

Patients with a cCa in the normal or near normal range preoperatively were significantly more likely to become hypocalcaemic than those who had a cCa of >2.8mmol/l ($p=0.005$). A preoperative cCa of >2.8mmol/l had a negative predictive value for postoperative hypocalcaemia requiring oral supplementation (<2.0mmol/l) of 94.8%.

There was no correlation between preoperative PTH and postoperative hypocalcaemia.

Conclusion

There was a significant correlation between normal or near normal preoperative calcium levels and postoperative hypocalcaemia. Patients with a preoperative calcium of greater than 2.8mmol/l could be considered for early discharge.

Determination of tumour cell fate in Multiple Endocrine Neoplasia Type 1-related tumours is dependent on menin and Bcl-2.

Mahsa Javid, Gerard V Walls, Jeshmi Jeyabalan, Anita AC Reed, Paul J Newey, M Andrew Nesbit and Rajesh V Thakker

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Multiple Endocrine Neoplasia Type 1 (MEN1) is characterised by the combined occurrence of pituitary, pancreatic and parathyroid tumours. The MEN1 gene encodes a tumour suppressor, menin, which has been shown by in vitro studies to have important roles in apoptosis and proliferation. We have investigated the in vivo role of menin in mice deleted for an Men1 allele, (Men1^{+/-}), which develop tumours due to a loss of menin. In Men1^{+/-} mice, tumour proliferation rates were up to 100-fold higher than in Men1^{+/+} normal tissue, $p < 0.0001$. Apoptotic rates were increased by two-fold in pituitary tumours compared with normal tissue (0.22% \pm 0.03 versus 0.12% \pm 0.03, $p = 0.02$), decreased in adrenocortical tumours (0.13% \pm 0.03 versus 0.61% \pm 0.07, $p < 0.0001$) and not significantly different in pancreatic and parathyroid tumours. To investigate the mechanisms underlying the observed increase in apoptosis in pituitary tumours we investigated genes involved in the extrinsic an

d intrinsic apoptotic pathways. Thus, genes involved in the extrinsic apoptotic pathway, including caspase 8, which is known to be regulated by menin, were downregulated in the tumours compared with wild-type. However, B-cell leukemia/lymphoma 2 (Bcl2), an important inhibitor of the intrinsic apoptotic pathway was also downregulated. Upregulation of the intrinsic pathway due to inhibition of Bcl2, therefore, may be a novel mechanism that regulates apoptosis in these tumours which have loss of menin yet increased apoptotic rates. These studies reveal an in vivo role of menin in the regulation of proliferation and apoptosis and suggest a role for Bcl2 in determining the fate of tumour cells.

Laparoscopic Adrenalectomy for Cases with big Tumours or Previous Laparotomy

Panagiotis B. Kekis(1,2), Haridimos Markogiannakis(1), Nikolaos V. Michalopoulos(1), Ioannis Flessas(1), Maria Natoudi(1), Emmanuel Evangelidakis(2), Maria Liparaki(2), George C. Zografos(1), Andreas Manouras(1)

(1) Department of Endocrine Surgery, 1st Department of Propaedeutic Surgery, Hippokration Hospital, University of Athens, Athens Medical School, Athens, Greece

(2) Athens Medical Centre, Athens, Greece

Aim: To evaluate the perioperative results of laparoscopic adrenalectomy for patients with big tumours or previous laparotomy. **Methods:** Prospective study of all patients undergoing laparoscopic adrenalectomy in our department between 2005 and 2009. **Results:** During the 5-year study period, 81 laparoscopic adrenalectomies were performed in 80 patients (mean age: 53.4 \pm 6.5 years, female: 61.2%). One case (1.2%) underwent bilateral adrenalectomy due to refractory Cushing's disease, 40 (50%) left and 39 (48.8%) right adrenalectomy. The most common final diagnoses in unilateral cases were non-functional adenoma (n=24, 30.3%), Conn's syndrome (n=15, 19%), Cushing's syndrome (n=15, 19%), pheochromocytoma (n=12, 15.2%) and solitary metastasis (n=8, 10.1%). Mean tumour diameter was 6.1 \pm 1.7cm (range: 1.5-10cm). Comparison between patients with a tumour >7cm (n=21, 26.3%) and those \leq 7cm (n=59) revealed no statistically significant difference in regards to age, sex, ASA physical status, body mass index, left/right adrenalectomy, operative or anaesthesia time, conversion to open adrenalectomy, postoperative feeding time, postoperative pain VAS scores at rest or at movement, analgesia requirements and consumption, complications, length of hospital stay and the final outcome (p>0.1). Similarly, no statistically significant differences were identified between cases with one or more previous laparotomies (n=25, 31.3%) and those without (n=55) (p>0.1). **Conclusion:** Laparoscopic adrenalectomy is safe and effective even for cases with big tumours or previous laparotomy.

Can Ultrasound Features be used to Predict Malignancy in Thyroid Nodule?

Gunasekaran S, Waqar-Huddin H, Khan K, Al-Zwae K, Ghosh S K, Martin-Hirsch D

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Introduction

Ultrasound (US) is the investigation of choice used in the assessment of thyroid nodule. Although, Fine needle aspiration cytology is essential, results vary and not necessarily predict the final histology. Recently it has been suggested that US findings such as solid nodule, hypoechogenicity, microcalcification, macrocalcification, ill-defined margins, intranodular vascularity, and taller-than-wide shape can be categorised to predict the potential of malignancy

Aim

To evaluate the characteristic US features in predicting malignancy

Settings/Method

Secondary care setting. Retrospective study one year period (Jan 2009 ? Dec 2009). Ultrasound features were compared with final histopathology report.

Results

48 cases were identified from the hospital radiology and histology database. 43 were female, 5 male. Mean age 51(21-82). 41 patients (85%) ultrasound features were correctly correlated to pathology, either benign or malignant. 9/41 were malignant and this was correctly suspected on ultrasound. The other 7 patient?s ultrasound features raised some suspicious features of malignancy but they were benign on histology. There were no malignancies missed on ultrasound findings

Conclusion

Categorisation of characteristic features on US of thyroid nodules can be helpful in predicting malignancy and helpful in decision making.

Free Papers Session 2

Friday 22nd November 10.45am to 11.45am

Chairs

Mr Johnathan Hubbard

Mr Jeremy Davis

Time Allocated per paper: 10mins

The effect of routine prophylactic calcium therapy post total thyroidectomy on frequency of hypocalcemia and length of hospital stay

Helen E Doran, Rahul Dwivedi, Iain D Anderson

Dept Surgery, Salford Royal Foundation Trust Hospital (SRFT)

Introduction: The effect of routine prophylactic calcium supplementation post total thyroidectomy on morbidity and length of stay was investigated.

Methods: Administration of routine prophylactic post-operative calcium supplementation to all patients undergoing total thyroidectomy independent of hypocalcaemia was introduced in November 2006. Hospital records 2004-2008 were reviewed grouping patients pre-prophylaxis and post-prophylaxis. Patients underwent 2 post-operative calcium level checks (normal range 2.1 \pm 0.2 mmol/L) with biochemical hypocalcaemia defined as < 2.1 mmol/L, clinical hypocalcaemia as paraesthetic symptoms with calcium level < 2.1 mmol/L.

Results: 86 pts underwent total thyroidectomy (16 male 70 female, mean age 50.1 years) by the same surgeon, pre-prophylaxis (n=59) post-prophylaxis (n=27). Mean number of hours post-op for first and second calcium levels were 18 and 36.5 hours. Incidence biochemical hypocalcaemia was 62.7% (37/59) pre-prophylaxis and 33.3% (9/27) post-prophylaxis. Incidence clinical hypocalcaemia was 20.3% (12/59) pre-prophylaxis and 14.8% (4/27) post-prophylaxis. Incidence clinical hypocalcaemia occurred in 4.6% (4/86), all pre-prophylaxis. Mean number of inpatient days was pre-prophylaxis group (2.81) compared to post-prophylaxis (2.56). Mean lowest post-operative calcium value was influenced by thyroid pathology: thyroid cancer (1.64mmol/L), thyrotoxicosis (2.06mmol/L) retrosternal goiter (2.08mmol/L) and simple goiter (2.13mmol/L), with no difference between the groups for thyroid pathology. No recurrent laryngeal nerve injury or post-operative haemorrhage occurred.

Discussion: Use of prophylactic calcium lowers the incidence of transient biochemical hypocalcaemia, reduced the frequency and severity of clinical hypocalcaemia and reduced length of post-operative stay.

PBF is induced by ionising radiation and functionally inactivates p53 in thyroid cancer

Seed RI, Sharma N, Fong JCW, Read ML, Lewy GD, Smith VE, Gentilin E, Kwan PPK, Ryan GA, Boelaert K, Franklyn JA, Watkinson JC and McCabe CJ

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PTTG is a multifunctional proto-oncogene overexpressed in thyroid cancers, which binds to p53 and modulates its function. PBF, a binding partner of PTTG, is also overexpressed in thyroid cancer and can transform cells independently of PTTG. Moreover, subcutaneous expression of PBF elicits tumours in nude mice. Given the established role of ionising radiation in thyroid tumourigenesis, we have investigated the relationship between PBF and the tumour suppressor protein p53. PBF repressed p53-mediated gene regulation through HDM2 promoter assays in p53-null H1299 cells.

Transfection of p53 elicited a 143 \pm 17-fold stimulation of promoter activity, whereas co-transfection of PBF significantly repressed p53 transcriptional activity (41 \pm 5-fold; $p < 0.001$). Exposure of wild-type mouse thyrocytes to gamma-irradiation resulted in a significant increase in PBF protein expression after 24 hrs (1.88-fold \pm 0.09-fold; $P < 0.017$). Co-immunoprecipitation assays revealed d

irect binding of PBF and p53 in human papillary thyroid carcinoma cells (hPTCs), with a marked increase in binding after treatment with gamma-irradiation. Furthermore, transient overexpression of PBF in hPTCs resulted in a marked decrease in p53 protein half-life compared to controls. Finally in MTT proliferation assays, we observed a significant reduction in cell viability of mock-transfected hPTCs after treatment with gamma-irradiation compared to untreated controls (17.9% \pm 0.008, $p < 0.016$, $n = 3$). Interestingly, overexpression of PBF prevented this observed decrease in cell viability (0.2% \pm 0.007, $p = \text{NS}$, $n = 3$). Taken together these data highlight a potential novel mechanism of thyroid tumourigenesis, whereby PBF stabilises in response to DNA damage, binds directly to p53 and inhibits its function.

Is minimally invasive thyroidectomy a realistic choice for the UK thyroid workload?

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Hammersmith Hospital

Introduction:

The inclusion criteria for minimally invasive thyroidectomy include; nodule size <3 cm, thyroid lobe volume of < 20mls, the absence of thyroiditis, previous neck surgery or radiation therapy. We examined the suitability for minimally invasive surgery of our routine caseload.

Methods:

100 consecutive thyroidectomies were retrospectively analysed. Patient demographics, indications for surgery and histological outcomes were recorded. Ultrasound measurements or pathological macroscopic dimensions were used to estimate thyroid lobe volume and maximum nodule diameter.

Results:

Of the 100 patients (82 female, median age 45 (range 18-81 years), a total of 54 hemithyroidectomies. 38 total thyroidectomies and 8 re-operative thyroidectomies were performed. Indications for surgery were (suspected) malignancy in 13, indeterminate cytology in 20 and the remainder for benign symptomatic pathology. The median nodule size and thyroid lobe volumes were 2.5 cm (range 0.7-6) and 64 mls (range 3.6-686.6) respectively

Of 100 thyroidectomies, 10 patients were potential candidates for a minimally invasive approach. The contraindications included:

Previous cervicotomy = 8

Thyroidectomy and lymphadenectomy = 5

Nodule size > 3cm = 10

Thyroid lobe volume > 20mls = 61 (which 20 also had evidence of thyroiditis)

Conclusion:

Even in a high volume unit, implementation of minimally invasive thyroidectomy techniques is hindered by the typical UK thyroid pathology and workload.

Positive pre-operative localisation scanning does not improve the likelihood of surgical cure in patients with primary hyperparathyroidism.

Michael J Stechman¹, Fergus V Gleeson², Radu Mihai¹, Gregory P Sadler¹.

¹Department of Endocrine Surgery, John Radcliffe Hospital, Oxford, UK.

²Department of Radiology, Churchill Hospital, Oxford, UK.

Background. Pre-operative localisation using ⁹⁹Tc-sestamibi and ultrasound in patients with primary hyperparathyroidism (PHPT) allows focused or minimally invasive parathyroidectomy (MIP) and is expected cure >95% patients. This prospective study aimed to determine whether negative pre-operative localisation is associated with reduced likelihood of post-operative normocalcaemia.

Methods. A prospective database was used to collect information on consecutive patients undergoing parathyroidectomy for sporadic PHPT in a tertiary centre.

Results. From January 2000-October 2009, 500 patients (359 women, median age 64, 17-90 years) had parathyroidectomy for PHPT. Patients were grouped according to localisation results: Group1 (n=290) - concordant sestamibi and neck ultrasound, Group2 (n=127) – negative scans and Group3 (n=83) - inconclusive scans. Group1 underwent MIP without intra-operative PTH measurement, and Groups2/3 underwent bilateral cervical exploration (n=210). Mediastinal adenomas were removed via sternotomy in 4 patients from Group3 following other localisation modalities. Tumours identified on imaging, were significantly larger than those not localised pre-operatively (P<0.001) and multi-gland disease was significantly less common in this group (P=0.012). Post-operative normocalcaemia was >95% in all 3 groups. During a median follow-up of 15 months (0-99 months) 17 patients had persistent disease and 3 patients developed recurrent disease (4%). Of these, 13 patients underwent a further 15 operations and 11 were cured. Currently 9 patients (1.8%) are known to have persistent disease.

Conclusion. Negative pre-operative localisation does not affect the outcome of parathyroidectomy in this unit. Persistent hypercalcaemia was <5% with or without localisation, and <2% after re-operative surgery. Those with positive localisation had larger tumours and a lower incidence of multi-gland disease.

Management of Cytologically Suspicious Thyroid Nodules (Thy4) for Malignancy.

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Department of Otolaryngology and Head and Neck Surgery, Guy's and St. Thomas' Hospitals, London, UK.

Background:

The aims of this study were to report our experience with patients with thyroid nodules cytologically classified as Thy4, and to describe and report the outcomes of different treatment approaches to cytologically suspicious thyroid nodules, and recommend a clinical management pathway

Methods:

Retrospective Case Review was conducted at a specialist Head and Neck Tertiary Referral Hospital over a period of 5 years

Results:

From 2005 to 2010 inclusive, 27 patients were referred with fine needle biopsies of thyroid nodules cytologically classified as suspicious for malignancy (Thy4). There were 25 females (92.6%) and 2 males (7.4%), with a mean age of 48 years (Range 23 to 84). Of these 27 Thy4 cases, 5 (18.5%) were downgraded to Thy3, 2 (7.4%) were upgraded to Thy5, and 1 (3.7%) was upgraded from Thy3. The diagnostic accuracy from fine needle biopsies classified as Thy4 for malignancy was 90%. Final histopathological diagnoses revealed 6 benign cases (22.2% - 4 of these 6 cases were downgraded from Thy4 to Thy3) and 21 malignant cases (77.7%), which included papillary thyroid cancer, medullary thyroid cancer, renal cell carcinoma, lymphoma and hyalinising trabecular carcinoma. Of the primary thyroid malignancies, 10 patients (52.6%) presented with Stage 1 disease, 5 patients with Stage 2 (26.3%), 3 patients with Stage 3 (15.8%), and 1 patient with Stage 4 (5.3%). Surgical treatment included lobe resection (8 cases), total thyroidectomy (11 cases), staged thyroidectomy (4 cases), revision thyroidectomy (2 cases), incisional biopsy (2 cases), with or without nodal clearance. Intraoperative frozen sections were used in 6 cases, with an overall diagnostic accuracy of 40%. Adjuvant radioactive iodine was administered to 17 patients. Overall survival was 93.1%.

Conclusions:

The overall diagnostic accuracy of cytologically classified Thy4 nodules for malignancy is high. Intraoperative frozen sections were not reliable for the diagnosis of thyroid malignancies. The surgical treatment of choice for cytologically suspicious thyroid nodules is a single stage total thyroidectomy with or without lymph node clearance, subject to patient consent.

Improving the rate of Minimally Invasive Parathyroidectomy : the impact of Surgeon-based Ultrasound

S. Nicholson, R. D. Bliss, T. W. J. Lennard, S. R. Aspinall

Newcastle upon Tyne Hospitals NHS Trust

Introduction: The potential advantages of minimally invasive parathyroidectomy (MIP) over bilateral neck exploration (BNE) are well described. The aim of this study was to establish the accuracy of imaging studies performed on patients with primary hyperparathyroidism (pHPT) referred to our unit and determine whether surgeon-based ultrasound (SUS) enabled more patients to undergo MIP.

Methods: A retrospective review of case notes from all patients who underwent parathyroidectomy in 2009 was undertaken. A Prospective study of 35 consecutive parathyroidectomies was then performed to evaluate SUS.

Results: 78 patients underwent parathyroidectomy in 2009. 54 were included in this study. 47/54 (87%) had single gland disease (SGD) of whom 19 (40%) had concordant localisation studies χ^2 see table 1.

% Neck US Sestamibi
Sensitivity 40 57
Specificity 89 88
Positive Predictive Value (PPV) 62 65
Accuracy 75 79

Table 1

SGD was present in 28/35 (80%) of the prospectively audited parathyroidectomies. SUS resulted in a trend towards greater co-localisation of parathyroid adenomas (21/28) versus (14/28) with neck US (p value 0.09 Fisher's exact) χ^2 see table 2.

% Neck US SUS P value χ^2 Fisher's exact
Sensitivity 42 78 0.002
Specificity 98 95 0.44
PPV 90 86 1.00
NPV 80 91 0.02
Accuracy 81 90 0.06

Table 2

Conclusions: SUS is more sensitive than pre-operative US and enables more patients with pHPT to benefit from MIP. Possible reasons for this include immediate intra-operative feedback allowing a quick learning curve and optimal placement of the patient's neck for SUS under anaesthesia.

Free Papers Session 3

British Journal of Surgery Prize Session



Chairs

Mr Chas Ubhi

Mr David Chadwick

Time Allocated per paper: 15 mins

Papers to be Judged On:

**Presentation
Scientific/Clinical Content
Impact
Ability to Answer Questions**

Judges

Datuk Dr Noor Hisham Bin Abdullah

Mr David Scott-Coombes

Mr Saba Balasubramanian

Men1 gene therapy using a modified adenovirus demonstrates reduced proliferation rates in murine Multiple Endocrine Neoplasia Type 1 pituitary tumours.

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Multiple Endocrine Neoplasia Type 1 (MEN1) is characterised by the combined occurrence of pituitary, pancreatic and parathyroid tumours. The MEN1 gene encodes a tumour suppressor, menin, and MEN1-associated tumours show loss of heterozygosity. This indicates that replacement of the wild type MEN1 gene may inhibit tumorigenesis. We report the results of a blinded randomised-controlled trial to assess the safety and efficacy of gene replacement in heterozygote (Men1^{+/-}) mice using a recombinant adenoviral vector. Men1^{+/-} female mice, aged 18.5 months, with pituitary tumours identified by MRI, were allocated to four groups. Anaesthetised mice received a 20µl transauricular intra-tumoral injection of vehicle, Ad-GFP or Ad-Men1 (5x10¹⁰ viral particles of recombinant adenoviral vectors delivering green fluorescent protein (GFP) or Men1 genes, respectively) or no injection. Mice received 1mg/ml 5-bromo-2-deoxyuridine (BrdU) in drinking water for four weeks post-injection before a repeat MRI scan. Fifty-eight of 153 scanned Men1^{+/-} mice had pituitary tumours. Mortality was similar in all groups (15% immediate, 18% late). GFP and menin expression were stable at four weeks. Daily proliferation rates revealed that Ad-Men1 treatment caused a significant reduction in tumour proliferation compared to the control groups. (0.45% \pm 0.09%, P<0.0001). Apoptotic rates and change in tumour volumes remained similar in the groups. Thus, in vivo Men1 gene replacement therapy for pituitary tumours was safe, demonstrated stable menin expression at four weeks and induced reduction of tumour proliferation. This establishes proof of concept for Men1 gene therapy and paves the way for studies to investigate such a treatment for pancreatic islet tumours.

Neck Ultrasound Referral Patterns In A Teaching Hospital and the Impact on Patients? Journey

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Background: Ultrasound assessment is an increasingly accepted tool in the work up of thyroid nodules, especially with FNAC (Lew et al 2010). However at what point in the patient journey the decision to scan should be made, remains controversial (Leil et al 2005).

Aim: To assess who was requesting neck ultrasounds, for what reason and how this altered the patients? journey.

Method: All neck ultrasound scans performed in 2009 were analysed for the referral origin, indication, time to scan, and need for specialist referral.

Results: Three hundred and eighty- four ultrasounds were performed in 2009. 167 scans (43%) were from primary care, 42 (11%) from other hospital departments and 175 (46%) from endocrine specialists. The indication for USS was thyroid abnormalities in 65% (250/384) of cases: 83 thyroid nodules; 127 goitres and 30 biochemical abnormalities. Primary care scans were performed in a median 35 days (0-70), while those newly referred by specialist endocrine surgeons took a median of 2 days (0-37). Following primary care ultrasound 43% (73/167) were referred in to hospital for specialist assessment: 61 to endocrine surgeons and 12 to endocrinologists. 31% (77/250) of thyroid patients required further ultrasound scans to establish a diagnosis prior to making a decision on management.

Conclusion: This study shows a significant number of primary care patients are inappropriately investigated with ultrasound prior to referral to a specialist thyroid rapid assessment clinic, resulting in duplication of scans and prolonged patient journey.

Serum phosphate predicts temporary hypocalcaemia after thyroidectomy

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Introduction: Acute hypocalcaemia occurs in up to 30% of patients following a total thyroidectomy. Post-operative serum calcium and parathyroid hormone (PTH) measurements are currently used to predict post-thyroidectomy hypocalcaemia. However, immediate access to PTH measurement is expensive and not widely available. Serum phosphate responds to changes in serum PTH levels within hours and its measurement is readily available in most hospitals. We evaluated the use of serum phosphate to predict temporary hypocalcaemia post-thyroidectomy.

Methods: We retrospectively identified 110 consecutive patients who had total/completion thyroidectomy and pre-operative serum calcium, phosphate, PTH and 25-hydroxyvitamin D measurements available. Patients had serum calcium, phosphate and PTH measured on the evening of surgery (day 0), on the morning of day 1 and over the following week as clinically indicated.

Results: 74 patients did not develop hypocalcaemia. In these patients, the mean serum phosphate fell overnight (as would be expected from the normal diurnal variation in serum phosphate). 17 patients who had a vitamin D >25nmol/l developed hypocalcaemia (calcium $\leq 1.95\text{mmol/l}$) from day 1 onwards and all had an overnight rise in serum phosphate to > 1.44mmol/l (100% sensitivity and specificity for predicting development of hypocalcaemia). 13 patients who had a vitamin D <25nmol/l also developed hypocalcaemia but as expected had an attenuated rise in serum phosphate likely due to hungry bone syndrome.

Conclusion: Serum phosphate is a reliable predictor of post-thyroidectomy hypocalcaemia in patients who do not have vitamin D deficiency and may facilitate day 1 discharge.

Ectopic hormone secreting pheochromocytoma: A francophone observational study

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Background

Ectopic hormone secreting pheochromocytomas are rare, only case reports exist in the literature. This condition has been linked with increased malignancy, familial syndromes and ACTH secretion. We wanted to test these hypotheses and shed light on the nature of ectopic hormone secreting pheochromocytomas.

Methods

This is a multi-centre (francophone) observational study. Inclusion was based upon abnormal pre-operative hormone tests in patients with pheochromocytoma that normalised after removal of the tumour. Where possible immuno-histochemistry was performed to confirm ectopic secretion came from the tumour.

Results

16 cases were found. There were 9 female and 7 male patients. Median age was 50.5 years (31-89). Most presented with hypertension, diabetes or cushingoid features. 10 patients had specific symptoms from the ectopic hormone secretion. Two had a familial syndrome. Of 8 patients with excess cortisol secretion, 3 died as a result of the tumour resection: 2 had pheochromocytomas >15cm and their associated cortisol hyper-secretion complicated their post-operative course, the other died from a torn sub hepatic vein. The 13 survivors didn't develop any evidence of malignancy during follow-up (median 50 mth). Symptoms from the ectopic secretion resolved after removal of the tumour. Immuno-histochemistry was performed and positive in 8 tumours: 5 ACTH, 3 calcitonin and 1 VIP.

Conclusions

Most pheochromocytomas with ectopic secretion are neither malignant nor familial. Excess cortisol secretion is the most frequent ectopic hormone. Patients with a pheochromocytoma should be worked up for ectopic hormones as removal of the pheochromocytoma resolves those symptoms. Associated cortisol secretion needs careful attention.

Management of the Thy2 Thyroid nodule

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British Thyroid Association guidelines advocate repeat FNAC for Thy2 thyroid nodules within 3-6 months in cases where a reliable benign diagnosis cannot be achieved. The recent introduction of 31 day cancer targets raises the question: What percentage of repeat FNAC for Thy2 turn out to be cancer and should this affect the timing of repeat FNAC? We present 5 years of thyroid FNAC at our institution.

Results:

393 primary FNAC of thyroid nodules were carried out between 2005 and 2010. The results were as follows: Thy1: 65(16.5%), Thy2: 240(61.1%), Thy3: 81(20.6%), Thy4: 3(0.8%), Thy5: 4(1.0%). 154 Thy2 were repeated, yielding Thy1: 19(12.3%), Thy2: 107(69.5%), Thy3: 26(16.9%), Thy4: 2(1.3%). The histology of the repeated Thy2 cases that became Thy3 or 4 was as follows: Multinodular goitre: 9(39.1%), Papillary carcinoma: 1(4.3%), Follicular carcinoma: 1(4.3%), Hurthle cell/ Follicular adenoma 12(52.2%). This compares with histology for Thy 3 at initial FNAC: Adenomas when initially Thy2 52.2%; when initially Thy3 49.4%; Carcinomas when initially Thy2 8.7%; when initially Thy3 19.5%, p=0.35.

Conclusions

Repeat FNAC for Thy2 nodules yielded Thy3 or higher in 18.2% of cases. Of these 52.2% were adenomas and 8.7% carcinomas. Our study supports repeating FNAC in Thy2 cases where a reliable benign diagnosis cannot be achieved. However, our study suggests that carcinoma is less common in Thy3 cases with previous Thy2 cytology. A carcinoma rate of 2/154(1.3%) in repeat FNAC for Thy2 suggests that rapid repeat of FNAC in order to meet 31 day cancer targets may be unnecessary.

The Role of Adrenal Vein Sampling (AVS) in the Diagnosis and Management of Primary Hyperaldosteronism : An Audit of Ten Years Experience at a Tertiary Referral Centre.

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Adrenal hypersecretion of aldosterone is a significant cause of secondary hypertension. Guidelines suggest that all potential adrenalectomy candidates should undergo adrenal venous sampling (AVS) to confirm unilaterality of secretion, due to the possibility of misleading findings on imaging alone. We present an audit of 41 cases of confirmed biochemical hyperaldosteronism dating back to 2000. All patients also had bilateral AVS and adrenal imaging.

Imaging identified adrenal lesions in 73% of patients. AVS confirmed lateralisation in 78% of patients. Imaging and AVS results were concordant in 68.8% of cases. Interesting examples of non-concordance are discussed in more detail. After work-up, patients were selected for either surgical (28/41) or medical (13/41) management. Age and gender were equally distributed across groups. Initial potassium requirements were greater in the surgical group (84 vs 48 mEq K+/day). Following surgery, antihypertensive burden fell from a mean of 2.7 to 1.2 drugs, and all patients were able to discontinue potassium supplements. In comparison, there was no reduction in the number of drugs taken after treatment optimisation for the medically-managed group, although overall blood pressure reduction was the same. We will also present follow up data on cardiovascular outcomes.

Our results reinforce the message that management of hyperaldosteronism in a tertiary referral centre alongside expertise in AVS is important due to the high rate of discordant imaging results. Where unilaterality of secretion has been confirmed, adrenalectomy is the optimal treatment because of a better reduction in medication burden and less need for long-term surveillance.

Reduced radioiodine uptake in a transgenic mouse model of human PTTG Binding Factor (PBF) over-expression

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PTTG Binding Factor (PBF) is a gene that is over-expressed in well-differentiated thyroid tumours. We recently report that PBF overexpression in-vitro can inhibit the activity of the sodium iodide symporter (NIS) which is responsible for iodide uptake into thyroid cells. The repression of NIS in thyroid cancer correlates with poor prognosis due to the importance of ^{131}I in the adjuvant treatment of thyroid tumours.

Methods

We have generated a murine FVB/N transgenic model of targeted over-expression of human PBF in the thyroid to investigate its biological role in vivo. Thyroid glands were harvested from age- and sex-matched wild-type (WT) and PBF homozygote mice. Thyroid glands from both WT and PBF mice were used for RNA extraction, histological section and primary murine thyroid culture.

Results

Real-time PCR analysis demonstrated a significant 48% reduction in NIS mRNA levels ($n=7$, $p<0.0001$) in transgenic murine PBF thyroids compared to WT. In parallel, NIS protein was reduced in PBF transgenic thyroids compared to WT, as determined by immunohistochemistry. Functional studies in primary murine thyroid cultures showed a 70.7% reduction in ^{125}I uptake in transgenic PBF compared to WT thyroid.

Discussion/Conclusion

This study verifies that previous observations of PBF function made in vitro are also apparent in vivo. Thus, targeted PBF over-expression in mice results in potent repression of NIS expression and function. The precise mechanism by which PBF represses NIS expression in vivo is currently being investigated. The critical importance of PBF in relation to NIS has direct implications in the use of radioiodine in the treatment of thyroid cancer.

Impact of routine ultrasound scanning on management of Thy3 cytology in dominant and isolated thyroid swellings ? a two centre comparative study.

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Introduction

Fine Needle Aspiration Cytology (FNAC) is the main investigation of thyroid swellings and reduces the operation rate . FNAC is limited by the proportion of Thy3 (indeterminate) cytology and ultrasound scanning (USS) has been widely adopted although its utility has not been rigorously assessed. An opportunistic study on the impact of USS was undertaken by comparing the outcome of management in patients with Thy3 aspirates between two centres with (A) and without (B) routine USS.

Methods

Retrospective analysis of prospectively collected data for the 5 years (2003-07) from two endocrine surgery centres. Data on patients with Thy3 cytology were compared.

Results

419 patients had 534 FNAC in A and 491 patients had 912 FNAC in B.

Thy 1 Thy 2 Thy 3 Thy 4 Thy 5

A 51 429 45 6 3

B 83 327 38 14 29

In Thy3 : males A: 9% vs B: 24% ($p=0.08$, χ^2). Mean age A: 46 years vs B: 59 years ($p<0.001$, t-test).

2 (4%) patients in each centre had cystic aspirates. Cytological features were similar between the centres. Thy3 diagnosis made on first FNAC in 71%(87% A; 53%B), second 22% (11% A; 34%B) with more FNAC to diagnosis in B ($p=0.007$, χ^2).

All patients in A had USS but only 7(14%) in B had any preoperative imaging ($p<0.001$, χ^2). No difference in distribution of size of swellings. All patients in A had surgery; 8 (21%) in B did not. Lobectomy performed in 39 (87%) in A vs. 23 (61%) in B, with total thyroidectomy in 6 (13%) vs. 7(18%) ($p=0.21$, χ^2) when non-operated cases excluded.

Pathology was malignant in 23 (28%); 16 (36%) in A and 7(18%) in B ($p=0.082$, χ^2), with follicular adenoma in 4 (9%) in A and 12 (32%) in B.

In A there was no difference between benign and malignant pathology on sonographic features of the swelling.

Discussion

There were interesting differences in practice. Fewer patients had Thy1 cytology in A but more had Thy4 & 5 in B. All patients in A with Thy3 underwent operation but only 79% in B. There were more cancers in the Thy3 group in A but this may relate to the smaller number of Thy4 & 5 reports. Ultrasound had no statistically significant impact on either selecting for or avoiding surgery in this study.

Two week wait thyroid cancer referrals have a low cancer yield

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Introduction:

The Two Week Waiting Time (2WW) Standard was introduced in 2000, and requires that patients with suspected cancer referred by general practitioners should be seen within 2 weeks. We reviewed the malignant yield of this referral modality in patients referred with suspected thyroid cancer.

Methods

We reviewed all the referrals sent as "two week waiters" from April 2009 to March 2010, to our one stop thyroid clinic. These referrals were evaluated for patient demographics, presenting complaint and diagnosis.

Results

23 patients were referred as "two week waiters" in the time period studied. All patients were seen within 2 weeks. Median patient age was 51 years, 18 were female. 14 patients were referred with a neck lump (58%), 8 with a solitary thyroid nodule (33%), 3 with hoarseness and 1 with a sore throat.. Combinations occurred in 4 cases. Of the 23 patients, 3 had malignant disease – 2 papillary thyroid cancers and one had squamous cell carcinoma. Sixteen patients (69%) had non-neoplastic pathology (colloid cysts (8); reactive lymphadenopathy (3); hashimoto's thyroiditis (1); submandibular calculus (1); lymphocytic thyroiditis (1), tuberculous lymphadenopathy (1); lipoma (1)). Four patients had no pathology demonstrable.

Conclusion: 3 of 23 patients referred under the 2-week rule had malignant tumours – 2 of these with thyroid cancer. 17 new thyroid cancers were diagnosed in the same clinic in the same time period and just 2 presented via the 2-week rule. The 2WW has a low cancer yield and may distort clinical priorities, disadvantaging patients from other referral pathways.

The Natural History of Nodular Goitre following Benign FNA: A 14 year Review of 2923 Patients

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BACKGROUND: Intervention for benign non-toxic thyroid nodules and/or goitre is determined by symptoms and patient preference. We explore the likelihood of later intervention following diagnosis of benign nodular goitre by clinical evaluation and fine needle aspiration cytology (FNAC)

METHODS: Retrospective study of cytology and pathology, if applicable, of patients presenting to a Teaching Hospital Thyroid FNAC clinic over 13 years. Outcome measures were re-referral for FNAC and/or surgery and incidence of differentiated thyroid cancer (DTC).

RESULTS: Between 1996 and 2009, 2923 patients (2402 Female, median age 51.4, 16-89 years) underwent FNAC for thyroid nodules: 390 were found to have THY3-5 cytology and were treated accordingly leaving 2533 patients with at least one benign FNAC (THY2). 218 (8.6%) patients had surgery for symptoms, and histology revealed incidental cancer in 14 patients (0.6%): five papillary (mean 26mm), six follicular (mean 50mm) and 3 micro carcinomas (mean 5.5mm). 2315 patients were treated expectantly. 902 (38.9%) returned for further evaluation a median of 6 years (1-13 years) later and had THY2 cytology. Of these, 249 (10.7%) underwent surgery for worsening symptoms. Final histology showed benign multi-nodular goitre with incidental cancer in 36 patients (1.56%): 13 papillary (mean 27mm), 12 follicular (mean 53mm) and 11 micro carcinomas (mean 5mm). The overall incidence of thyroid cancer in those with benign FNAC that had surgery was 2.66 per 1000, per year.

CONCLUSION: Expectant management of non-toxic nodular goitre is safe with a low incidence of incidental cancers. However, over a third of those treated return for re-evaluation and eight percent eventually undergo surgery.

Posters to Be Presented

BJS Prize for best British Trainee Poster

Thyroid Carcinoma in Retro Sternal Goitre

Urinary free catecholamines and free methyl derivatives in the diagnosis of catecholamine secreting tumours

Preoperative and intraoperative predictive factors of postoperative hypocalcaemia after parathyroid adenoma resection

Parathyroid Imaging: Is more than one modality always required?

The Increasing Role of Central Lymph Node Dissection in Differentiated Thyroid Cancer

The feasibility of day-case thyroid surgery: a review of 17 years of practice

Variations in TSH Post Thyroid Lobectomy

A systematic review and meta-analysis of the role of sentinel node biopsy in papillary thyroid cancer

Multinodular goitres causing obstructive sleep apnoea syndrome

Audit of length of stay and the cost implications associated with use of drains in thyroid surgery. An evidence based approach

Surgery for the recurrent non-toxic goitre: a case-control study

An overview of the management and outcome of thyroid cancers in a district general hospital

An interesting case of multifocal accessory thyroid tissue: a review of literature

Biochemical diagnosis of Pheochromocytoma/paragangliomas: the need for comprehensive testing

The Medway Mini Thyroid Guide

The Lower the Goitre the Higher the Cut - The Management of Retrosternal Goitre

Review of minimally invasive video assisted thyroid surgery

The Evolution of Parathyroid Surgery

Correlation Between Clinical Diagnosis, FNAC and Final Histological Diagnosis, of Thyroid Masses