Diagnostic yield of ultrasound-guided fine needle aspiration biopsy (US-guided FNAB) and post-surgical histopathological correlation of thyroid nodules in the Department of Radiology, Groote Schuur Hospital, Cape Town, South Africa over a two-year period.

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A research report submitted to the

Faculty of Health Sciences, University of Cape Town,

in fulfilment of the requirements for the degree of

Master of Medicine in Diagnostic Radiology

Declaration

I, BORNAVENTURE MATIMATI hereby declare that the work on which this dissertation/thesis is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

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Acknowledgements, format, and contributions

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This thesis is written in a publication-ready format and is intended for publication in the South African Journal of Radiology (SAJR).

Table of Contents

Abstract

Background: Nodular thyroid disease is common worldwide, and the incidence of thyroid nodules is increasing globally. Ultrasound (US)-guided thyroid nodule fine needle aspiration biopsy (FNAB) is a reliable and cost-effective method of distinguishing between benign and malignant nodules before major surgery is performed.

Aims: The study aimed to establish the diagnostic yield of US-guided thyroid FNAB's done at Groote Schuur Hospital over two years and to correlate findings with histopathological results in those patients that underwent thyroidectomy.

Objectives: The objectives were to establish the number of US-guided FNABs performed, the number of repeat FNABs and the number of patients who subsequently had thyroidectomy over two years. A further objective was to evaluate the diagnostic yield by comparing the cytology and histology results for patients that underwent thyroidectomy.

Methods: This was a retrospective study of all patients referred for US-guided FNAB from 1 January 2018 to 31 December 2019. All patients with cytology results after FNAB and histology results after thyroidectomy, were included in the study. US-guided FNAB data was collected from the Picture Archiving and Communication System (PACS) and Radiology Information System (RIS), while cytology and histology data were obtained from the National Health Laboratory Services (NHLS).

Results: A total of 236 patients were included in the study (220 females and 16 males), with ages ranging from 19 to 82 years. The diagnostic yield was 34-% on the first, 36-% on the second and 48-% on the third FNAB. Most of the US-guided FNABs were non-diagnostic (66-% on the first, 64-% on the second and 52-% on the third FNAB). A total of 107 patients (45 %) had a repeat FNAB, while 23 patients (9.7-%) had a second repeat FNAB. A total of 48 patients (20.3-%) underwent thyroidectomy. Cancer was detected in 29/236 (12.3-%), of which 17/29 (59-%) were papillary thyroid carcinomas. There was no significant correlation between FNAB results and post-surgical histopathological results in patients who underwent thyroidectomy, with a p value of .15.

Conclusion: The overall cancer rate of 12.3-% was comparable with that of other institutions. 66-% of US-guided FNABs were non-diagnostic, while 34-% were diagnostic on the first FNAB with 45-% requiring a repeat second FNAB. The assistance of a cytopathologist during the biopsy has been known to result in fewer non-diagnostic results, avoiding repeat attempts. Further diagnostic and cost-effective analysis of cytopathology assistance in the US-guided FNAB for characterising thyroid nodules is advised.

Chapter 1: Literature Review

Background and epidemiology

The incidence of thyroid nodules is rising globally. The worldwide prevalence of multinodular goitre (MNG) in the general population is estimated to be 4-7-% and these lesions are often caused by iodine deficiency [1], [2]. The World Health Organization estimates at least 1.6 billion people are at risk of iodine deficiency disorders, and of these, 655 million are affected by goitre [1]. MNG usually presents as an anterior neck mass. Other smaller thyroid nodules may be detected incidentally during clinical or ultrasound evaluation of the neck [2]. Thyroid nodules are detectable in 5-% of the normal population on clinical examination, over 48-% on high-resolution ultrasound and over 50-% at autopsy [3].

The prevalence of palpable thyroid nodules is approximately 5-% in women and 1% in men in iodine-sufficient parts of the world [4]. This goes up to 19-% - 68-% of randomly selected individuals with high-resolution ultrasound with higher frequencies in women and the elderly [4]. Thyroid cancer, however, remains a rare disease with an incidence of only 1 - 2/100 000 population per year [3], and represents the most common malignancy of the endocrine system [5].

A definite diagnosis of either nodular disease or cancer is challenging to make [3]. Multinodular goitre has been thought to have a lower risk for malignancy than single-nodule goitre [6]. Papillary and follicular carcinoma have good long-term prognosis and survival rates, while anaplastic and medullary subtypes have a poorer prognosis and shorter survival [3].

Role of ultrasonography

Every patient with a palpable thyroid nodule is a potential candidate for fine needle aspiration biopsy (FNAB) and should undergo further evaluation to determine whether FNAB is warranted [7]. The selection of patients for US-guided FNAB of thyroid nodules is primarily determined by assessing ultrasound findings in patients with asymptomatic thyroid nodules [8]. Ultrasound enables the investigation of 'suspicious' nodules based on the following specific criteria: mixed echogenicity (cancer being hypoechoic), micro-calcifications, spiculated, micro-lobulated or irregular borders, an anteroposterior diameter greater than the transverse diameter, increased intra-nodular blood flow, and the presence of a nodule 'halo' on Doppler flow study [2], [9], see Fig 1.

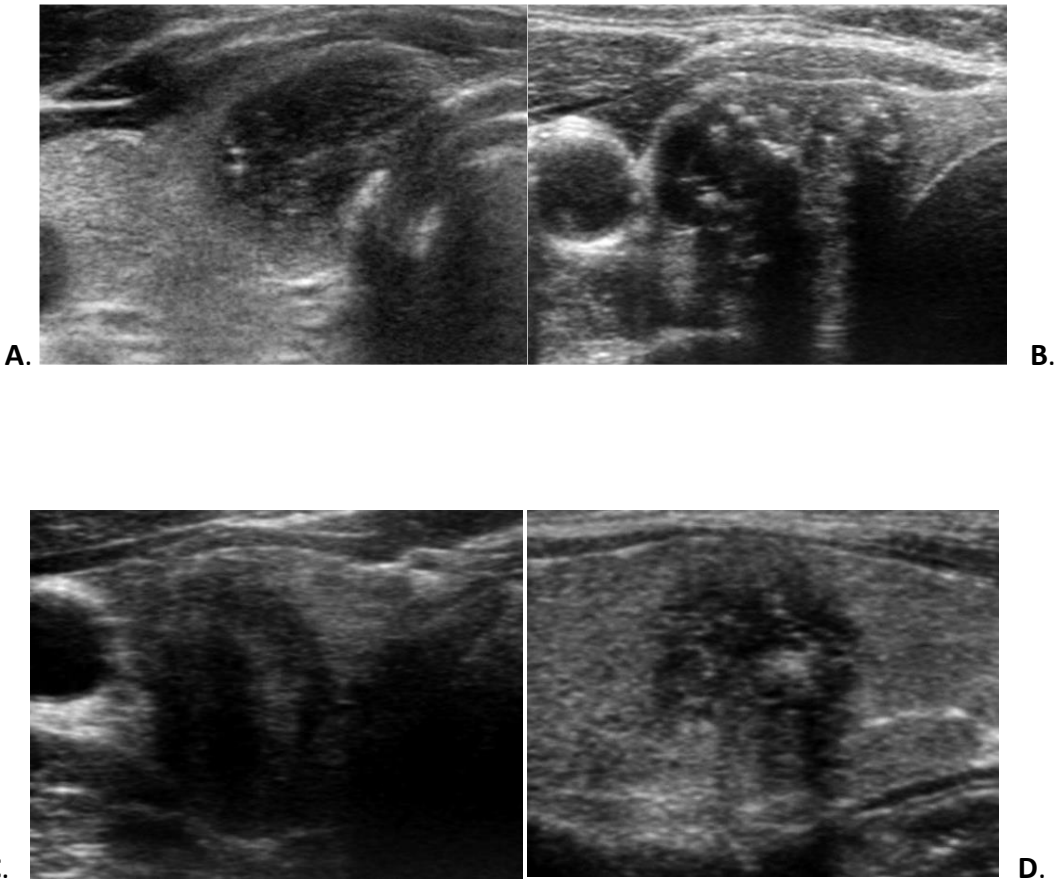


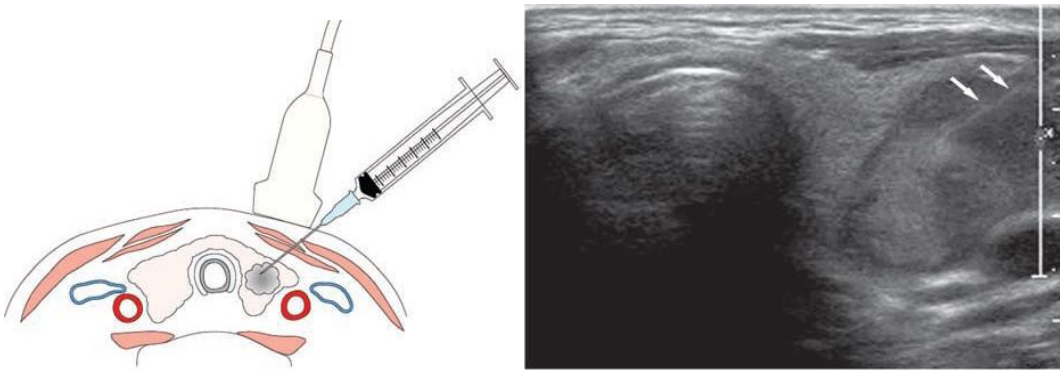
Fig 1: A. Solid hypoechoic nodule with microcalcifications. **B.** Solid hypoechoic nodule with micro and macrocalcifications. **C.** Solid hypoechoic nodule with non-parallel orientation (taller than wide). **D.** Solid hypoechoic nodule with spiculated/micro lobulated margin [8].

Extra-thyroidal extension (ETE) of the primary tumour is a risk factor for tumour recurrence and mortality, occurring in 11.5–30-% of differentiated thyroid carcinomas [8]. Ultrasound features predictive of the ETE include capsular protrusion, disruption, and abutment [8]. Recent advances in US-guided FNAB have improved pre-operative diagnosis of nodules in many centres [3]. Practice guidelines suggest that an initial FNAB is cost-effective and reliable and is now believed to be the most effective preoperative method for distinguishing between benign and malignant thyroid nodules [10].

Before performing an US-guided thyroid FNAB, a complete history and physical examination should be performed, and serum thyrotropin level (TSH) and thyroid US should be obtained [11]. Risk factors for malignancy include previous head and neck and total body irradiation, family history of thyroid cancer, firm or hard nodule, hoarseness or vocal cord paralysis, cervical lymphadenopathy, and invasion of surrounding tissues with fixation [7]. The incidence of malignancy in functioning thyroid nodules is very low and nodules that demonstrate decreased function on radionuclide scan should be correlated with ultrasound for FNAB [7], [11].

Ultrasound-guided FNAB technique

The patient is placed in a supine position with the neck slightly extended with a pillow under the shoulders. After the lesion is localized, and allergy excluded, the overlying skin is cleansed with a 10% povidone-iodine solution, and the area is draped. A high-resolution (7.5–15-MHz) linear-array transducer, with a sterile cover placed over its head is used for ultrasound [12].



A. **B.**

Fig 2: (a) Schematic diagram demonstrating needle position in a nodule **(b)** US image demonstrating needle positioned as in **a**, showing the needle within the nodule (white arrows) [12].

Using povidone-iodine solution for skin sterilization negates the need for coupling gel as it serves as a coupling agent [12]. Local anaesthesia allows repeated aspiration and ice can also be used as it has a dual effect of causing numbness and constricting the vessels, thus reducing haemodilution [12]. Thinner needles have been reported to have a better yield of cytologic material [12]. Prior ultrasound evaluation with Doppler mapping helps prevent intra-procedural vascular injury, and two acquisition methods are widely used: aspiration, and non-aspiration [12]. The non-aspiration technique is useful in hyper vascular nodules as it reduces the probability of obtaining a bloody specimen [12]. The collected material is placed on glass slides, smeared, and fixed in 95% ethyl alcohol [12]. Post-procedure management includes applying a pressure dressing to the biopsy site and instructing the patient to visit the nearest emergency centre if there is increasing swelling or worsening pain [12]. Indications for repeat FNA include inadequate sampling, enlarging nodules on follow-up imaging, cyst recurrence and imaging findings suspicious of malignancy [12].

Clinical relevance in local setting

Although other factors can cause MNG, persistent iodine deficiency cannot be ruled out, as despite the iodination of table salt since 1982, the iodine content in different brands of salt available in shops in South Africa varies [2], [13]. The most common thyroid cancer worldwide is papillary carcinoma (80%) [2]. Follicular carcinoma however remains the most

frequently diagnosed thyroid malignancy in black South Africans and the rest of the African continent [13]. Nodular thyroid disease has benefitted from the proliferation of diagnostic methods, which should be cost-effective and provide quality care to the patient [10]. However, in their study, Cairncross and Panieri concluded that their institution was performing below the pre-operative diagnosis and therapy planning standards achieved in international multidisciplinary units [3].

Conclusion

The routine use of US-guided FNAB has profoundly changed the management of thyroid nodules. FNAB allows prompt identification and treatment of thyroid malignancies whilst avoiding unnecessary surgery in patients with benign lesions, thereby improving the overall quality of life for patients with thyroid nodules.

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Chapter 2: Full Text Journal Article for Submission

Cover Letter

Full Title:

Diagnostic yield of ultrasound-guided fine needle aspiration biopsy (US-guided FNAB) and post-surgical histopathological correlation of thyroid nodules in the Department of Radiology, Groote Schuur Hospital, Cape Town, South Africa over a two-year period.

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Source(s) of support: No grant other than from UCT for statistical support.

Authors' contributions:

- Identifying research question and objectives with supervisor
- Literature review, collection and recording of data
- Liaison with statistician for data analysis and summary
- Discussion of results and write-up with guidance from supervisor

Supervisor's contributions:

- Guidance on research question and proposal
- Supervision and provision on patient data
- Provision of relevant literature
- Revision of initial protocol, literature review and manuscript

Disclaimer: All views expressed in this article are our own and not an official position of the institution or funder.

Word Count:

Abstract: 427

Article: 2053

Pages: 37

Abbreviations:

GSH - Groote Schuur Hospital

FNAB – Fine needle aspiration biopsy

PACS – Picture Archiving and Communication System

RIS – Radiology Information System

NHLS – National Health Laboratory Services

ACR-TIRADS – American College of Radiology Thyroid Imaging and Reporting Data System

US – Ultrasound

Graphs, tables, and Images:

Title: **Diagnostic yield of ultrasound-guided fine needle aspiration biopsy (US-guided FNAB) and post-surgical histopathological correlation of thyroid nodules in the Department of Radiology, Groote Schuur Hospital, Cape Town, South Africa over a two-year period.**

Abstract:

Background: Nodular thyroid disease is common worldwide, and the incidence of thyroid nodules is increasing globally. Ultrasound-guided thyroid nodule fine needle aspiration biopsy (FNAB) is a reliable and cost-effective method of distinguishing between benign and malignant nodules before major surgery is performed.

Aims: The study aimed to establish the diagnostic yield of US-guided thyroid FNABs done at Groote Schuur Hospital over two years and to correlate the findings with histopathological results in those patients that underwent thyroidectomy.

Objectives: The objectives were to establish the number of US guided FNABs performed, the number of repeat FNABs, and the number of patients who subsequently underwent thyroidectomy over two years. A further objective was to evaluate the diagnostic yield by comparing the cytology and histology results for patients that underwent thyroidectomy.

Methods: This was a retrospective study of all patients referred for US-guided FNAB from 1 January 2018 to 31 December 2019. All patients with cytology results after FNAB and histology results after thyroidectomy, were included in the study. US-guided FNAB data was collected from the Picture Archiving and Communication System (PACS) and Radiology Information System (RIS), while cytology and histology data were obtained from the National Health Laboratory Services (NHLS).

Results: A total of 236 patients were included in the study (220 females and 16 males), with ages ranging from 19 to 82 years. The diagnostic yield was 34-% on the first, 36-% on the second and 48-% on the third FNAB. Most of the US-guided FNABs were non-diagnostic (66-% on the first, 64-% on the second and 52-% on the third FNAB). A total of 107 patients (45-%) had repeat FNAB while 23 patients (9.7-%) had a second repeat FNAB. A total of 48

patients (20.3-%) underwent thyroidectomy. Cancer was detected in 29/236 (12.3-%) of which 17/29 (59-%) were papillary thyroid carcinomas. There was no significant correlation between FNAB results and post-surgical histopathological results in patients who underwent thyroidectomy, with a p value of 0.15 at significance level alpha 0.05.

Conclusion: The overall cancer rate of 12.3 % was comparable with that of other institutions. This study identified a high rate of non-diagnostic US-guided FNABs. Sixty six percent of US-guided FNAB's were non-diagnostic at the first attempt. The presence of a cytopathologist during the biopsy has been shown to result in fewer non-diagnostic results, therefore, avoiding repeat attempts. The presence of a cytopathologist during diagnostic thyroid nodule US-guided biopsies in our clinic should be explored from a cost perspective as this could possibly lead to fewer repeat biopsies with the resultant benefit to the patients and hospital.

Introduction

The incidence of thyroid nodules is rising globally. According to the World Health Organization, at least 1.6 billion people are at risk of iodine deficiency disorders, and of these, 655 million are affected by goitre [1]. Follicular carcinoma remains the most frequently diagnosed thyroid malignancy in black South Africans and the rest of the African continent despite iodinated table salt since 1982 [2], [13]. Although other factors cause MNG, persistent iodine deficiency cannot be ruled out as the iodine content in different brands of salt available in shops in South Africa varies [2].

The study will assess the diagnostic yield of ultrasound-guided fine needle aspiration biopsy of thyroid nodules in the Department of Radiology at Groote Schuur Hospital, a tertiary hospital in the Western Cape Province of South Africa. The goal of an initial sonographic assessment of thyroid nodules is to distinguish benign nodules that can be managed conservatively from those with suspicious or malignant features requiring further management [14]. The performance of FNAB needs to be selective, since FNAB of all nodules, regardless of the size or appearance, is superfluous and may even lead to unnecessary diagnostic thyroid surgery [14].

Reports comparing the effectiveness of specific, defined training strategies for FNAB procurement are lacking and there is little agreement on the definition of adequate training [11]. There is evidence that when FNA specimen procurement is concentrated in fewer hands and when the same physician both procures and microscopically examines the specimen, the results improve [11]. In their study at Groote Schuur Hospital, Cairncross and Panieri (2013) concluded that the institution was performing below international multidisciplinary unit standards in achieving pre-operative diagnoses to better plan therapy [3]. Their key recommendations for better diagnostic accuracy included improved US reports, FNAB sampling techniques and cytopathology reporting [3].

This study will help to assess if there has been any significant improvement in the use of US-guidance in thyroid FNAB at Groote Schuur Hospital. It seeks to establish the diagnostic yield of US-guided thyroid FNABs and correlate the findings with histopathological results in those patients that underwent thyroidectomy. The study will establish the number of US-guided FNABs performed, number of repeat FNABs and the number of patients who subsequently underwent thyroidectomy over the two years. It will also compare the cytology and histology results for patients that underwent thyroidectomy.

Research methods and study design

The study was a retrospective review of patient ultrasound images and FNAB results. All patients that were referred for US-guided FNAB of thyroid nodules from the 1 January 2018 to 31 of December 2019 to the Department of Radiology, Groote Schuur Hospital, were reviewed. The study included only patients who underwent US-guided FNAB and had cytology results on NHLS. Patients who had corresponding histology results were presumed to have undergone thyroidectomy. The study excluded patients who had US-guided FNAB but no cytology results on NHLS, those who had thyroidectomy without prior US-guided FNAB and those who had core biopsy of thyroid nodules.

Materials and methods

The patients were referred to the US Department for US-guided FNAB of suspicious thyroid nodules. All patients had a baseline ultrasound examination of the thyroid gland and suspicious nodules were graded using the American College of Radiology Thyroid Imaging and Reporting Data System (ACR-TIRADS), see Fig 3. The system graded nodules based on five characteristics: composition, echogenicity, shape, margin, and echogenic foci. Depending on the score, nodules were graded into five TIRAD groups. TIRADS 1 and 2 were considered benign and were not considered for US-guided FNAB. TIRADS 3 nodules were biopsied if greater than or equal to 2.5 cm. TIRADS 4 nodules were biopsied if greater than or equal to 1.5 cm while TIRADS 5 nodules were biopsied if greater than or equal to 1 cm in diameter.

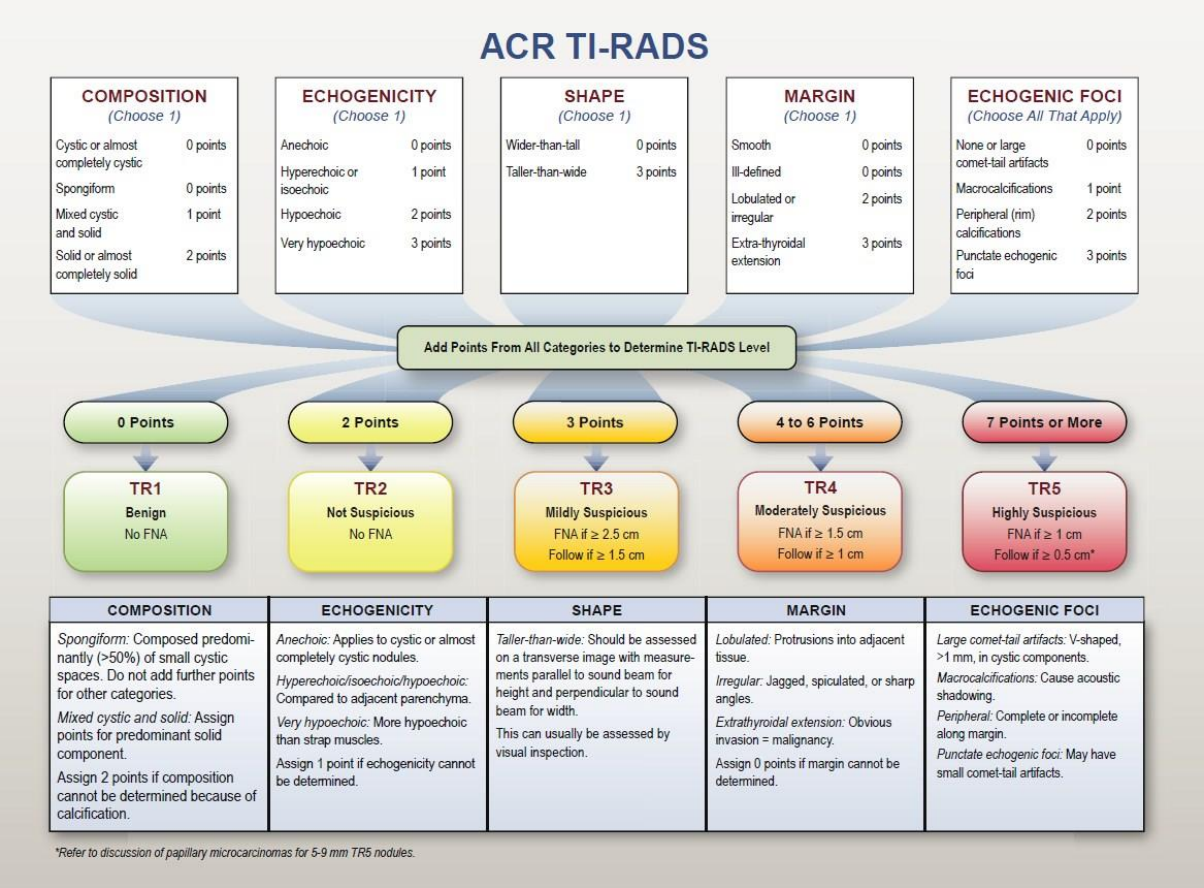

Fig 3: ACR-TIRADS [15]**.**

The procedure was performed by a consultant radiologist or radiology registrar in the ultrasound department. A 7.5 – 15-MHz linear array transducer of a Toshiba ultrasound scanner was used to visualise and target suspicious nodules using a 22 – 27 Gauge needle. The specimen was obtained by capillary action, and then smeared on slides. The sample was fixed using Cytofix and air-dried before being taken to the laboratory for cytological assessment. The Bethesda system for reporting thyroid cytopathology was used to report the findings, see Fig 4.

Diagnostic category	Description	Risk of malignancy (%)
I	Non-diagnostic/unsatisfactory	1–4
II	Benign	0–3
III	Atypia or follicular lesion of undetermined significance	5–15
IV	Follicular neoplasm or suspicious for follicular neoplasm	15–30
V	Suspicious for malignancy	60–75
VI	Malignant	97–99

Source: Cibas ES, Ali SZ. The 2017 Bethesda system for reporting thyroid cytopathology. J Am Soc Cytopathol. 2017;6:217–222. https://doi.org/10.1016/j.jasc.2017.09.002

Fig 4: Bethesda System [16].

All procedures were performed as day procedures and patients were discharged after the procedure. A sterile dressing was applied to the biopsy site and patients were advised to return to the hospital if there was increasing swelling, pain, or bleeding.

Data collection

Patient US images were viewed on PACS and the indication for the US and the imaging findings were documented. Patient thyroid function test, cytology and histology results were obtained from NHLS, and the data was entered on a password-protected Excel spreadsheet.

Data analysis

The data was presented using histograms, bar charts and tables, and analysed using Statistical Package for Social Sciences (SPSS). A chi-square test was performed on the data to ascertain any correlation between the cytology and histology results.

Ethical considerations

Ethical approval was granted by the Human Research Ethics Committee of the University of Cape Town, HREC Ref 253/2020 (Addendum A) and permission was obtained from Groote Schuur Hospital (Addendum B).

Results

A total of 236 patients were included in the study of which 220 were females (93 %) and 16 were males (7%). The patient ages ranged from 19 to 82 years with median age of 56 years and interquartile range of 19 years.

All patients had at least one ultrasound-guided FNAB, and those with a non-diagnostic result (Bethesda 1) were offered a repeat biopsy. Some patients did not return for repeat FNAB, and of those who did, some were recalled for yet another repeat FNAB if the results of the second biopsy were non-diagnostic.

Of the 236 patients with FNAB, 155 (66%) were non-diagnostic (Bethesda 1), 41(17%) patients had a benign result (Bethesda 2), while 18 (8%) patients were Bethesda 3 (atypia or follicular lesion of undetermined significance). A total of 22 (9%) patients were Bethesda 4 - 6, see Fig 5.

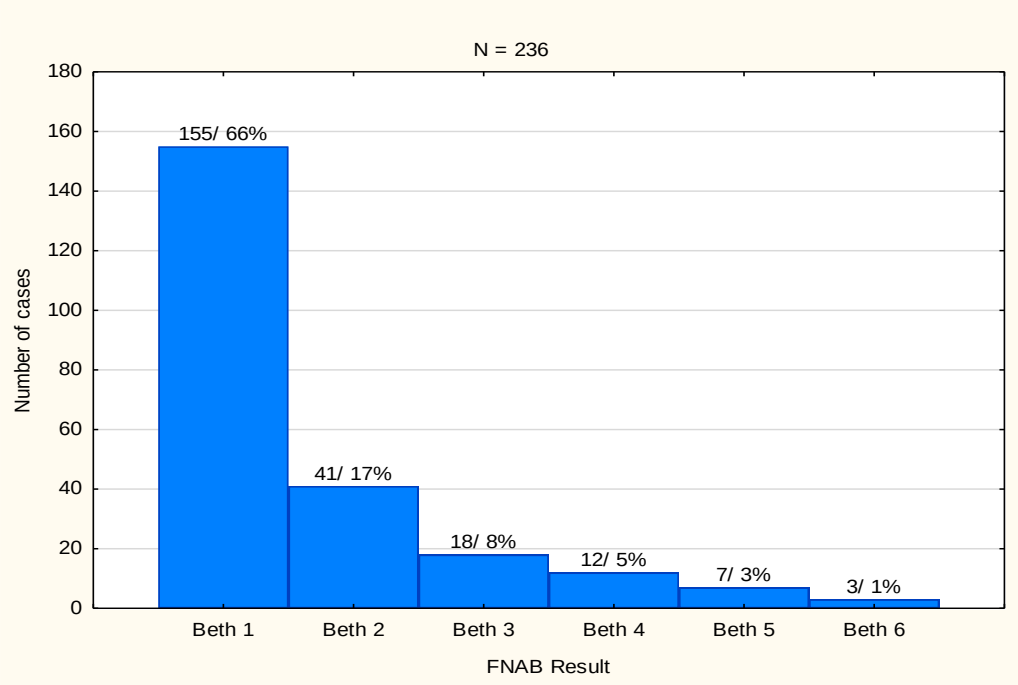

Fig 5 : Bethesda results after first FNAB

All patients (155) whose results were non-diagnostic after the first FNAB were recalled for repeat FNAB, of which 107 attended. Sixty eight (64-%) patients had non-diagnostic results (Bethesda 1), while seventeen (16-%) had benign results (Bethesda 2), see Fig 6.

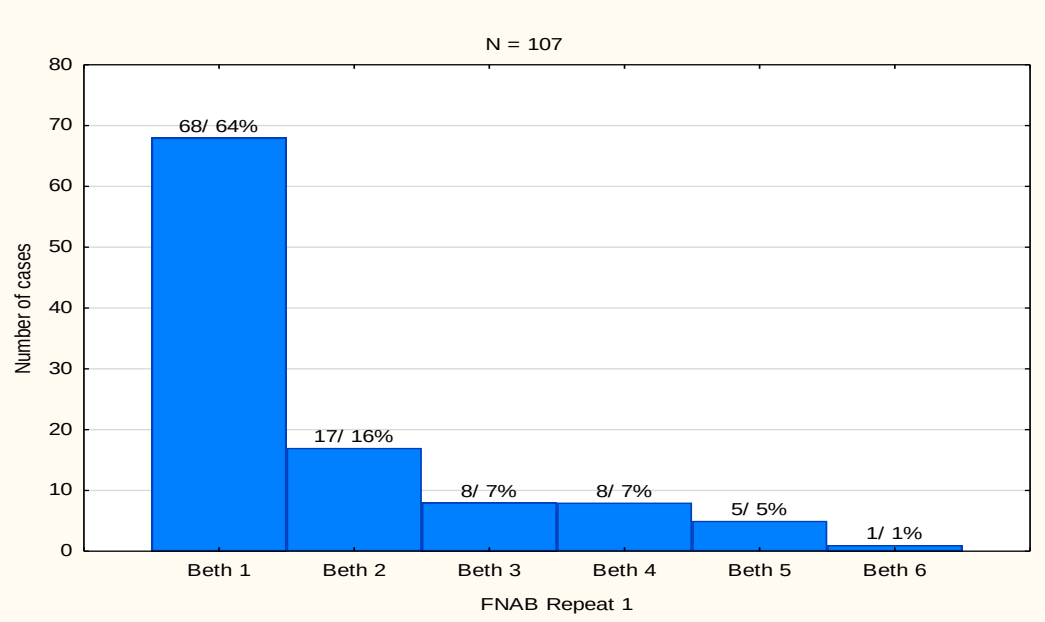

Fig 6: Bethesda results after second FNAB

Sixty eight patients with non-diagnostic results on the second FNAB were recalled for a third FNAB, of which 23 attended. Twelve (52-%) patients had non-diagnostic results (Bethesda 1), while one patient (4-%) had a benign result (Bethesda 2), see Fig 7.

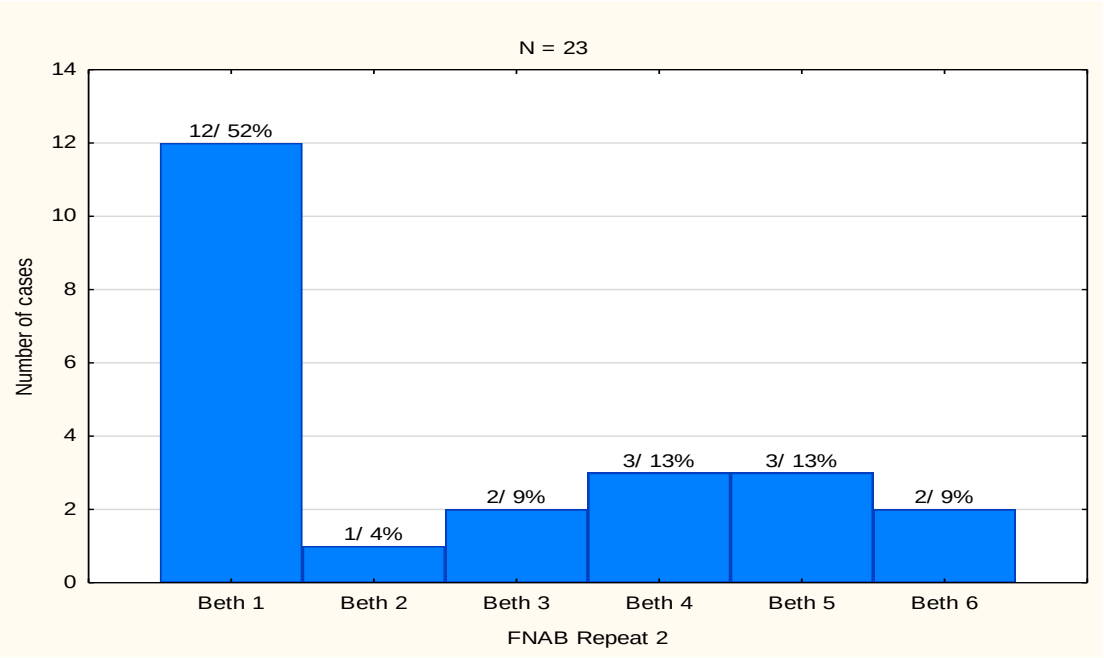

Fig 7 : Bethesda results after third FNAB.

Forty-eight patients underwent thyroidectomy for various reasons including suspicious FNAB results and the majority (60%) had malignant histology results, see Table 1.

Bethesda Category (FNAB)	Benign Histology	Malignant Histology
Bethesda 1	7 (15%)	6 (12%)
Bethesda 2-3	5 (10%)	4 (8%)
Bethesda 4-6	7 (15%)	19 (40%)
Total	**19 (40%)**	**29 (60%)**

Table 1: Histology results vs Bethesda Classification

Although there was a greater proportion of malignant histology results in the Bethesda 4-6 category, there was no significant correlation between increasing Bethesda classification and malignant histology results at significance level alpha 0.05, p value = 0.15.

Most confirmed cancers were papillary thyroid carcinoma, 17 (59-%), Fig 8. One patient had confirmed lung adenocarcinoma and the thyroid nodule was a metastatic deposit. Three patients had Non-invasive Follicular Thyroid neoplasm with Papillary-like nuclear features (NIFTP). This has been reclassified recently as a benign lesion but at the time of study it was considered a premalignant condition managed with thyroidectomy, hence its inclusion on the histogram

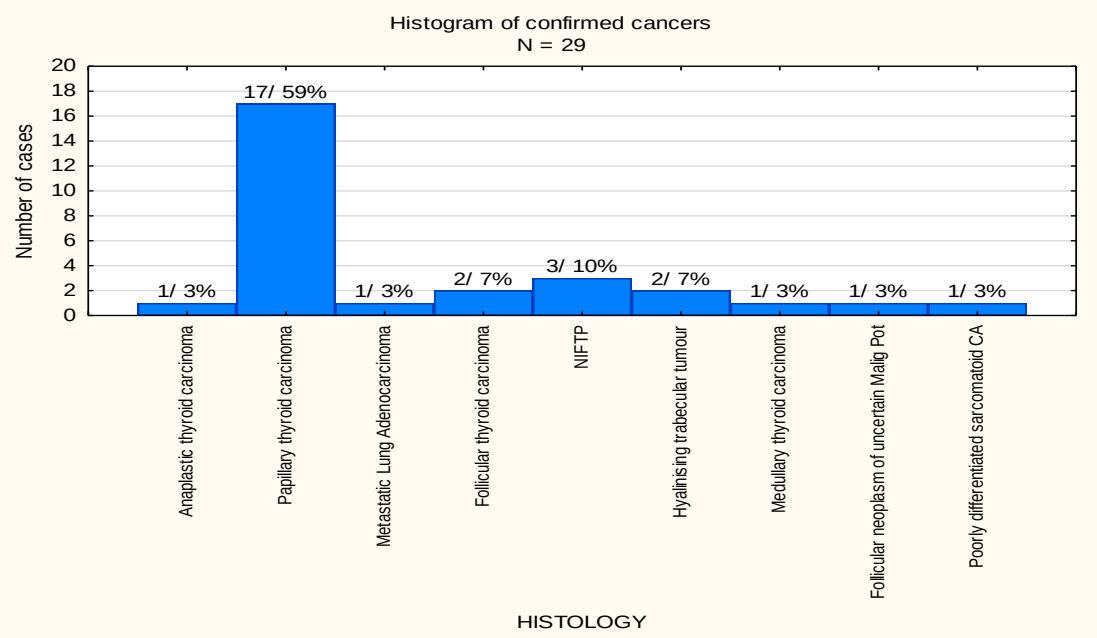

Fig 8: Histology results of confirmed cancer

Most benign histology results 13 (72%), were multinodular goitre. Two patients had Hashimoto's thyroiditis, see Fig 9.

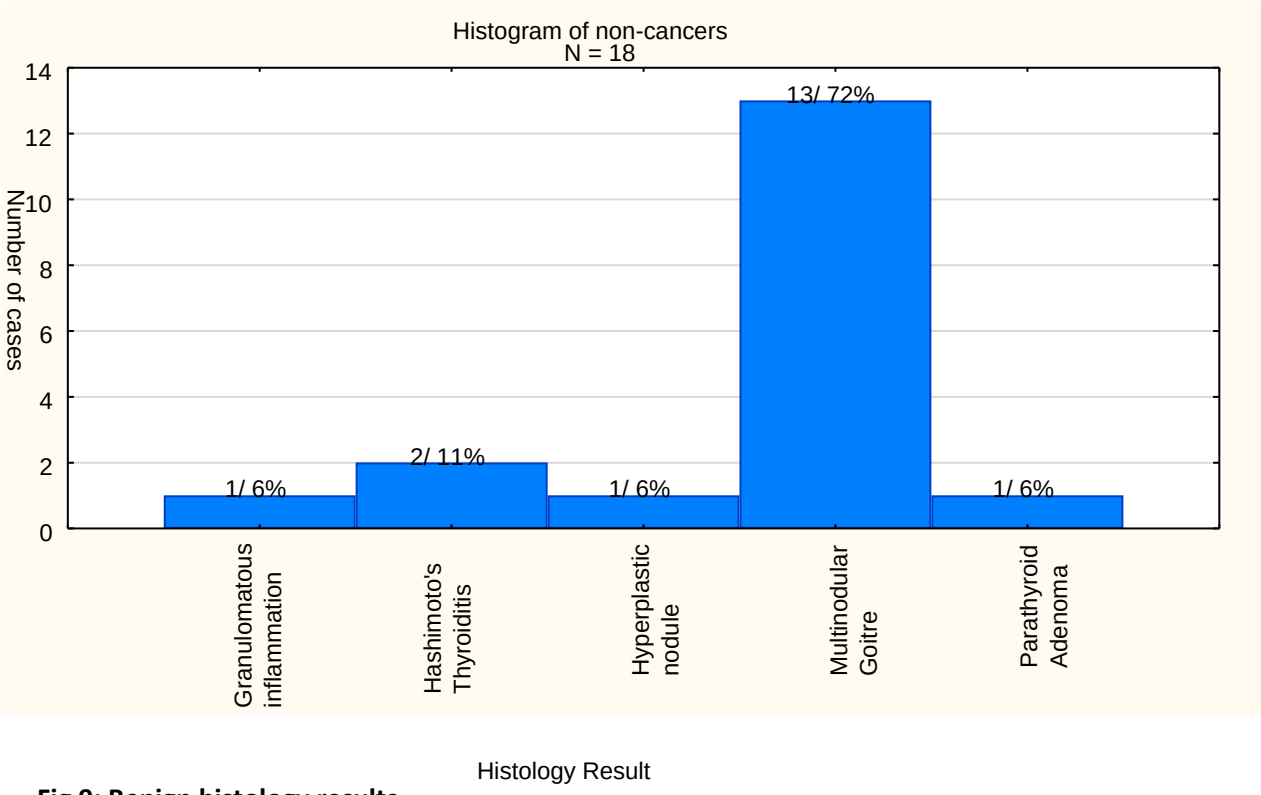

Fig 9: Benign histology results

Discussion:

The majority of the ultrasound-guided FNABs in our study were non-diagnostic. Several studies have indicated that 70-98% of patients with non-diagnostic FNABs had benign lesions, with a low incidence of neoplasia (5-10%) after histopathological diagnosis [10]. However, these non-diagnostic FNABs could also be partly attributed to the relative inexperience of the radiology registrars performing the biopsies. FNABs were undertaken during their training block in ultrasound and often the largest dominant and not necessarily most ultrasonographically suspicious nodule was biopsied [3]. Another possible cause for the inadequacy of specimens obtained, especially from larger nodules, is that large nodules are more often cystic and contain necrotic areas as found in a study by Degirmenci et al [12].

A further potential source/cause of non-diagnostic FNABs may be a non-standardised slide preparation technique. In order to develop and maintain the necessary level of staff expertise at GSH, the number of staff members who perform FNABs and the interpreting cytologists should be kept small [12], or alternatively, more formalised training could be considered. A supervised training of registrars in US-guided FNAB of thyroid nodules during their ultrasound block may minimise the number of patients with Bethesda 1 results and therefore having to undergo a repeat FNAB. Optimal results of thyroid nodule FNAB can be achieved by performing aspiration at least twice where the aspiration technique is used and utilising the non-aspiration technique on hyper-vascular nodules where there is a higher probability of aspirating blood [12].

The majority of benign histology results were multinodular goitre (72%) which differed from the Polokwane study in which multinodular goitre was second to adenoma [1]. The overall cancer rate in our study was 12 % which was similar to the prevalence rate reported in the Polokwane study [1]. In a Korean study the rate of malignancy was 5-15% among nodules detected by palpation, while it was 8-12% among non-palpable nodules evaluated by FNA [8]. Papillary thyroid carcinoma constituted the majority of malignant results (7.2%) which

was similar to the Polokwane study in which 7.8% had papillary thyroid carcinoma [1]. Palo et al also found that classical type papillary thyroid carcinoma was the commonest malignancy in their study [5].

The majority of patients in our study were females (93%) with males constituting 7 %. The age range was from 19 to 82 years with a median age of 56 years. The findings were similar to the Polokwane Mankweng Hospital complex study where females constituted 94.4% and the age range was from 4 to 80 years with a mean age of 45 years [1]. The age and gender distribution was also similar to other studies in Kenya and East Africa [10]. The indications for surgery included suspicious FNAB results, pressure symptoms and cosmetic reasons. There was no significant correlation between FNAB cytology and post-surgical histopathological results in patients who had thyroidectomy, after a chi square test at alpha level 0.05 gave a p value of 0.15.

The assistance of a cytopathologist results in fewer non-diagnostic results thus avoiding repetition of the procedure albeit at a higher cost [17]. A study to assess diagnostic value and cost effectiveness of onsite cytopathology in US-guided FNAB for characterising thyroid nodules is recommended. The findings of such a study may provide medical managers with documented evidence supporting inclusion of the cytopathologist's assistance in thyroid nodule FNAB if available resources permit. This should result in a decrease in the number of repeated procedures, diminishing time to diagnosis and minimise patient discomfort. This is especially crucial if the risks of a delayed diagnosis in malignancy and the patient's psychological comfort are taken into consideration.

Strengths and Limitations

This retrospective study benefitted from using data already available on the PACS and NHLS systems. A limitation was that the study considered patients to have undergone thyroidectomy only if their histology results were on the NHLS lab system. It excluded patients who might have had FNAB at Groote Schuur Hospital and thyroidectomy at a private institution.

Conclusion:

Most of thyroid FNAB results were Bethesda 1 (non-diagnostic) on the initial biopsy and on subsequent biopsies for patients who were recalled for repeat FNAB. The overall cancer rate was comparable to other institutions supporting the belief that most patients with non-diagnostic FNAB have benign lesions. There was no significant correlation between FNAB and histology results in patients who subsequently underwent thyroidectomy. It is recommended the presence of a cytopathologist during US-guided FNAB be explored to establish if it would result in a decrease in the number of non-diagnostic and repeated procedures.

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Addendum A: Ethics Approval

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room G50- Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6492
Email: hrec-enquiries@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

18 May 2020

HREC REF: 253/2020

Dr N Ahmed
Radiation Medicine /Radiology
J-Block-GSH
Email: redhot007_za@yahoo.com

Dear Dr Ahmed

PROJECT TITLE: DIAGNOSTIC YIELD OF ULTRASOUND GUIDED FINE NEEDLE ASPIRATION BIOPSY AND POST-SURGICAL HISTOPATHOLOGICAL CORRELATION OF THYROID NODULES IN THE DEPARTMENT OF RADIOLOGY, GROOTE SCHUUR HOSPITAL, CAPE TOWN, SOUTH AFRICA, OVER A TWO-YEAR PERIOD -MMED-CANDIDATE -DR BORNAVENTURE MATIMATI

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee (HREC) for review.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

This approval is subject to strict adherence to the HREC recommendations regarding research involving human participants during COVID -19, dated 17 March 2020.

Approval is granted for one year until the 30 May 2021.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

We acknowledge that the student: Dr Bonaventure Matimati will also be involved in this study

Please quote the HREC REF in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval, where necessary, before the research may occur.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE

HREC 253/2020sa

Addendum A: Ethics Approval

HUMAN RESEARCH ETHICS COMMITTEE
- 3 JAN 2022
HEALTH SCIENCES FACULTY
UNIVERSITY OF CAPE TOWN

UNIVERSITY OF CAPE TOWN — FACULTY OF HEALTH SCIENCES
Human Research Ethics Committee

FHS016: Annual Progress Report / Renewal

HREC office use only (FWA00001637; IRB00001938) This serves as notification of annual approval, including any documentation described below.			
☑ Approved	Annual progress report	Approved until/next renewal date	30.01.2023
☐ Not approved	See attached comment		
Signature Chairperson of the HREC/ Designee		Date Signed	12/1/22

Note: Please email this form and supporting documents (if applicable) in a combined pdf-file to hrec-enquiries@uct.ac.za.
Please clarify your plan for research-related activities during COVID-19 lockdown.
Please use the latest form found on our website:
http://www.health.uct.ac.za/fhs/research/humanethics/forms

Comments to PI from the HREC
"Thank you for your Study Deviation Signature: Date: 12/1/22

Principal Investigator to complete the follc

1. Protocol Information

Date (when submitting this form)	13 DECEMBER 2021		
HREC REF Number	253/2020	Current Ethics Approval was granted until	30 MAY 2021
Protocol title	DIAGNOSTIC YIELD OF ULTRASOUND GUIDED FINE NEEDLE ASPIRATION BIOPSY (US-FNAB) AND POST-SURGICAL HISTOPATHOLOGICAL CORRELATION OF THYROID NODULES IN THE DEPARTMENT OF RADIOLOGY, GROOTE SCHUUR HOSPITAL, CAPE TOWN, SOUTH AFRICA, OVER A TWO-YEAR PERIOD		
Protocol number (if applicable)	N/A		
Are there any sub-studies linked to this study?		☐ Yes	X No
If yes, could you please provide the HREC Reference number for all sub-studies? **Note:** A separate FHS016 must be submitted for each sub-study.	N/A		

(Note: Please complete the Closure form (FHS010) if the study is completed within the approval period)

Addendum B: Hospital Approval

GROOTE SCHUUR HOSPITAL
Enquiries: Dr Bernadette Eick
e-mail: Bernadette.Eick@westerncape.gov.za

Dr Nazier Ahmed
RADIOLOGY

E-mail: redhot007@yahoo.com / drmatimati@gmail.com

Dear Dr Ahmed,

RESEARCH PROJECT: Diagnostic Yield Of Ultrasound Guided Fine Needle Aspiration Biopsy And Post-Surgical Histopathological Correlation Of Thyroid Nodules In The Department Of Radiology, Groote Schuur Hospital, Cape Town, South Africa, Over A Two-Year Period. (MMed Dr Bornaventure Matimati)

Your recent letter to the hospital refers.

You are granted permission to proceed with your research, which is valid until **30 May 2021.**

Please note the following:

a) Your research may not interfere with normal patient care.
b) Hospital staff may not be asked to assist with the research.
c) No additional costs to the hospital should be incurred i.e. Lab, consumables or stationary. **If access to TRACK Care/NHLS is required, kindly attach our letter of approval to the application form.**
d) **No patient folders may be removed from the premises or be inaccessible.**
e) Please provide the research assistant/field worker with a copy of this letter as verification of approval.
f) Confidentiality must always be maintained .
g) Should you at any time require photographs of your subjects, please obtain the necessary indemnity forms from our Public Relations Office (E45 OMB or ext. 2187/2188).
h) Should you require additional research time beyond the stipulated expiry date, please apply for an extension.
i) Please discuss the study with the HOD before commencing.
j) Please introduce yourself to the person in charge of an area before commencing.
k) On completion of your research, please forward any recommendations/findings that can be beneficial to use to take further action that may inform redevelopment of future policy / review guidelines.
l) Please contact Michelle Riley (Patient Fees) at ext. 2276 to ascertain if there will be charges for conducting the Research and to obtain a quote or to discuss charges
m) Kindly submit a copy of the publication or report to this office on completion of the research.
n) At no time should any posters encouraging patients to partake in research, be displayed within a clinical area.

I would like to wish you every success with the project.

Yours sincerely

DR BERNADETTE EICK
CHIEF OPERATIONAL OFFICER
Date: 29 May 2020

C.C. Mr. L. Naidoo, Dr H. Aziz. Dr S. Moosa

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South African Journal of Radiology Instructions to Authors

Original Research Article full structure

Title: The article's full title should contain a maximum of 95 characters (including spaces).

Abstract: The abstract, written in English, should be no longer than 250 words and must be written in the past tense. The abstract should give a succinct account of the objectives, methods, results and significance of the matter. The structured abstract for an Original Research article should consist of five paragraphs labelled Background, Objectives, Method, Results and Conclusion.

- Background: Why do we care about the problem? State the context and purpose of the study. (What practical, scientific or theoretical gap is your research filling?)

- Objectives: What problem are you trying to solve? What is the scope of your work (e.g. is it a generalised approach or for a specific situation)? Be careful not to use too much jargon.

- Method: How did you go about solving or making progress on the problem? State how the study was performed and which statistical tests were used. (What did you actually do to get the results?) Clearly express the basic design of the study; name or briefly describe the basic methodology used without going into excessive detail. Be sure to indicate the key techniques used.

- Results: What is the answer? Present the main findings (that is, as a result of completing the procedure or study, state what you have learnt, invented or created). Identify trends, relative change or differences on answers to questions.

- Conclusion: What are the implications of your answer? Briefly summarise any potential implications. (What are the larger implications of your findings, especially for the problem or gap identified in your motivation?) Do not cite references and do not use abbreviations excessively in the abstract.

Introduction: The introduction must contain your argument for the social and scientific value of the study, as well as the aim and objectives:

Social value: The first part of the introduction should make a clear and logical argument for the importance or relevance of the study. Your argument should be supported by use of evidence from the literature.

Scientific value: The second part of the introduction should make a clear and logical argument for the originality of the study. This should include a summary of what is already known about the research question or specific topic, and should clarify the knowledge gap that this study will address. Your argument should be supported by use of evidence from the literature.

Conceptual framework: In some research articles it will also be important to describe the underlying theoretical basis for the research and how these theories are linked together in a conceptual framework. The theoretical evidence used to construct the conceptual framework should be referenced from the literature.

Aim and objectives: The introduction should conclude with a clear summary of the aim and objectives of this study.

Research methods and design: This must address the following:

Study design: An outline of the type of study design.

Setting: A description of the setting for the study; for example, the type of community from which the participants came or the nature of the health system and services in which the study is conducted.

Study population and sampling strategy: Describe the study population and any inclusion or exclusion criteria. Describe the intended sample size and your sample size calculation or justification. Describe the sampling strategy used. Describe in practical terms how this was implemented.

Intervention (if appropriate): If there were intervention and comparison groups, describe the intervention in detail and what happened to the comparison groups.

Data collection: Define the data collection tools that were used and their validity. Describe in practical terms how data were collected, and any key issues involved, e.g., language barriers.

Data analysis: Describe how data were captured, checked, and cleaned. Describe the analysis process, for example, the statistical tests used, or steps followed in qualitative data analysis.

Ethical considerations: Approval must have been obtained for all studies from the author's institution or other relevant ethics committee and the institution's name and permit numbers should be stated here.

Results: Present the results of your study in a logical sequence that addresses the aim and objectives of your study. Use tables and figures as required to present your findings. Use quotations as required to establish your interpretation of qualitative data. All units should conform to the SI convention and be abbreviated accordingly. Metric units and their international symbols are used throughout, as is the decimal point (not the decimal comma).

Discussion: The discussion section should address the following four elements:

- Key findings: Summarise the key findings without reiterating details of the results.
- Discussion of key findings: Explain how the key findings relate to previous research or to existing knowledge, practice, or policy.
- Strengths and limitations: Describe the strengths and limitations of your methods and what the reader should consider when interpreting your results.
- Implications or recommendations: State the implications of your study or recommendations for future research (questions that remain unanswered), policy or practice. Make sure that the recommendations flow directly from your findings.

Conclusion: Provide a brief conclusion that summarises the results and their meaning or significance in relation to each objective of the study.

Acknowledgements: Those who contributed to the work but do not meet our authorship criteria should be listed in the Acknowledgments with a description of the contribution. Authors are responsible for ensuring that anyone named in the Acknowledgments agrees to be named. Refer to the acknowledgement structure guide on our Formatting Requirements page. Also provide the following, each under their own heading:

Competing interests: This section should list specific competing interests associated with any of the authors. If authors declare that no competing interests exist, the article will include a statement to this effect: The authors declare that they have no financial or personal relationship(s) that may have inappropriately influenced them in writing this article. Read our policy on competing interests.

Author contributions: All authors must meet the criteria for authorship as outlined in the authorship policy and author contribution statement policies.

Funding: Provide information on funding if relevant

Data availability: All research articles are encouraged to have a data availability statement.

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