

## The diagnostic ability of core needle biopsy in nodular thyroid disease

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### ABSTRACT

**INTRODUCTION** Non-diagnostic results of fine needle aspiration biopsy (FNAB) remain an important limitation of this technique. The aim of our study was to evaluate the results of core needle biopsy (CNB) of thyroid nodules and its effectiveness in non-diagnostic FNAB cases.

**METHODS** CNBs were performed in 1,000 patients (154 male, 846 female; mean age: 50.2 years, range: 18–86 years) with a spring loaded 20G needle. Of these, 143 had initially had FNABs that were insufficient for evaluation. The CNB reports were reviewed. Patients with suspicious or malignant CNB results underwent total thyroidectomy.

**RESULTS** When considering all 1,000 CNBs, the non-diagnostic rate was 1.5% (15/1,000). However, when the first 100 cases were eliminated as a learning curve, this reduced to 0.9% (8/900). Of the 143 cases with initial FNABs that were non-diagnostic, 0.7% (1/143) were also non-diagnostic on CNB. Twelve patients underwent surgery because of malignant CNB reports and all of these cases were confirmed as malignant by the postoperative pathology specimen results (100% accuracy). There were no major complications although three self-limiting minor complications were observed.

**CONCLUSIONS** CNB is a safe and accurate method. It is more diagnostic than FNAB for nodular thyroid disease.

### KEYWORDS

Core needle biopsy – Thyroid – Nodule – Fine needle aspiration

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Thyroid disease is the most frequent endocrine disorder<sup>1</sup> and the incidence of thyroid nodules is very high.<sup>2</sup> Most thyroid nodules are benign but some require treatment because of the risk of malignant transformation, cosmetic reasons or subjective symptoms.<sup>3</sup> Thyroid malignancies are the most common endocrine cancers<sup>4</sup> although less than 5% of these nodules are malignant.<sup>2</sup>

Fine needle aspiration biopsy (FNAB) of thyroid nodules has been used for more than 50 years and is an effective method for evaluating nodules.<sup>5</sup> However, non-diagnostic results of FNAB remain an important limitation.<sup>6</sup> Approximately 10–30% of FNAB samples have indeterminate cytological results that make the management of these nodules more difficult.<sup>7,8</sup> Even though repeated FNABs have non-diagnostic result rates of 17–47%,<sup>9–12</sup> current guidelines recommend repeating FNAB for indeterminate cases.<sup>13</sup>

Ultrasonography guided core needle biopsy (CNB) for nodular thyroid disease is useful for cases with non-diagnostic FNAB results and atypia of uncertain significance at FNAB.<sup>12</sup> Several studies suggest that CNB might be a promising alternative to repeated FNAB for thyroid nodules with initially non-diagnostic FNAB results but there is no consensus on this issue.<sup>14–16</sup> Some authors have reported better

results with a combination of FNAB and CNB<sup>17</sup> while others have found no difference between the diagnostic accuracy of FNAB and CNB.<sup>5,18</sup> The aim of our study was to evaluate the results of CNB in a large clinical series in terms of its effectiveness in non-diagnostic FNAB cases.

### Methods

Subsequent to local ethics committee approval and obtaining informed consent, a group of 1,000 patients (154 male, 846 female; mean age: 50.2 years, range: 18–86 years) were enrolled in the study. All patients were admitted to our endocrine surgery outpatient clinic between January 2013 and September 2015. The inclusion criteria for the study were: age >18 years, euthyroid condition, nodule size >1cm, ultrasonography and/or clinical findings suspicious for thyroid cancer and an initial FNAB that was reported as non-diagnostic (insufficient for evaluation) in another centre. Patients who refused CNB were excluded.

CNB was performed under local anaesthesia with real time ultrasonography guidance, using a linear probe (12–5MHz) with an iU22® device (Philips, Amsterdam, Netherlands). A surgeon with more than 15 years of experience in

thyroid biopsies performed all procedures. A spring loaded 20G full core Monopty® biopsy needle (Bard, Tempe, AZ, US) was used. The needle was 9cm long and had a penetration depth of 11mm.

Patients were placed in the supine position with the neck extended. After an ultrasonography evaluation to identify the thyroid nodule of interest, 1% lidocaine was injected into the subcutaneous tissue. The ultrasonography probe was placed over the nodule and the biopsy needle was inserted with ultrasonography guidance to the edge of the nodule. The approach was usually transisthmic but depending on the nodule's location, the biopsy needle was sometimes inserted directly through the nodule. Two or three CNB specimens were typically taken for each nodule. If a nodule was cystic, the intranodular content was aspirated before carrying out the CNB using a 22G device. Patients were discharged after firm local compression of one minute.

The biopsy material was put in cups with formalin and transferred to the pathology unit. Histopathological evaluation was performed by an experienced pathologist using haematoxylin and eosin. The pathology reports were divided into six categories as per the British Thyroid Association classification: Thy1 (non-diagnostic), Thy2 (non-neoplastic), Thy3a (atypical features present), Thy3f (follicular neoplasm suspected), Thy4 (suspicious of malignancy) and Thy5 (diagnostic of malignancy).<sup>19</sup>

If the CNB pathology results were Thy3a, Thy3f, Thy4 or Thy5, patients underwent total thyroidectomy and the reports of the pathology specimens were reviewed. Non-diagnostic FNAB results were compared with the subsequent CNB results. The main evaluation parameter in this study was the diagnostic value of CNB.

## Results

The mean nodule diameter was 19.3mm (range: 10–45mm). The non-diagnostic rate for all 1,000 CNBs was 1.5% (Table 1). The first 100 cases were considered to represent a learning curve; 7 of these were non-diagnostic. Among the last 900 cases, there were 8 non-diagnostic reports (0.9%) (Table 2). The CNB reports revealed only one non-diagnostic result (0.7%) among the 143 initial FNABs that were non-diagnostic (Table 3).

Twelve patients with malignant pathology on the CNB reports underwent total thyroidectomy. Malignant CNB reports were revealed to be 100% accurate on specimen pathology: papillary carcinoma in ten cases (83.3%), medullary carcinoma in one case (8.3%) and anaplastic carcinoma in one case (8.3%). Of the samples with Thy3a, Thy3f and Thy4 CNB pathology results, 20 (71.4%) were benign and 8 (28.6%) were malignant.

There were no major complications although three minor complications were noted. Swallowing problems were observed in two patients; one had a self-limiting intranodular haematoma and the other had a haematoma near the paravertebral muscles. The other minor complication was a self-limiting subcutaneous haematoma. All of the minor complications improved without the need of medication and/or hospitalisation.

**Table 1** Classification of core needle biopsy pathology reports of all 1,000 cases

Report	n
Thy 1	15 (1.5%)
Thy 2	945 (94.5%)
Thy 3a	9 (0.9%)
Thy 3f	13 (1.3%)
Thy 4	6 (0.6%)
Thy 5	12 (1.2%)

**Table 2** Classification of core needle biopsy pathology reports of last 900 cases

Report	n
Thy 1	8 (0.9%)
Thy 2	858 (95.3%)
Thy 3a	8 (0.9%)
Thy 3f	11 (1.2%)
Thy 4	5 (0.5%)
Thy 5	10 (1.1%)

**Table 3** Classification of core needle biopsy pathology reports of cases with initial non-diagnostic fine needle aspiration (n=143)

Report	n
Thy 1	1 (0.7%)
Thy 2	138 (96.5%)
Thy 3a	1 (0.7%)
Thy 3f	2 (1.4%)
Thy 4	0 (0%)
Thy 5	1 (0.7%)

## Discussion

The incidence of thyroid nodules is very high and management could be difficult in some cases. FNAB is the most frequently used method for diagnosis of nodular thyroid disease. However, a non-diagnostic result is an important limitation of FNAB.<sup>6</sup> CNB might be a promising alternative diagnostic method to overcome this limitation.

Our department has been performing CNB routinely since 2013 for thyroid nodules that are larger than 1cm and in cases where initial FNAB at another centre is non-diagnostic. Management decisions are still made based on biopsy

results and are not influenced by the type of biopsy. All patients with Thy3a, Thy3f, Thy4 or Thy5 results undergo total thyroidectomy

### Published literature

Silverman *et al* reviewed 309 FNABs of thyroid nodules in 295 patients performed by one endocrinologist between 1979 and 1984.<sup>5</sup> In 23 of these patients, a large needle biopsy ( $n=16$ ) or core biopsy ( $n=10$ ) was also carried. Eight patients underwent thyroidectomy after the biopsy. Among these, the results of all of the FNABs and six of the eight tissue biopsies showed agreement with the surgical specimen; there was no statistically significant difference between the groups.

Stangierski *et al* performed 30 CNBs and 59 FNABs in patients with nodular goitre.<sup>18</sup> CNBs were carried out using 22G and FNABs with 25G needles. In total, 56.6% of the CNBs and 50.8% of the FNABs were diagnostic; there was no statistically significant difference between the groups. Sixty per cent of the patients considered the pain of CNB to be similar to that experienced during the previous FNAB whereas forty per cent felt that the CNB pain was more intense. There were no complications in either of the groups. The authors concluded that CNB was more expensive than FNAB but that there was no difference in diagnostic effectiveness.

In a retrospective study by Choi *et al*, the results of 180 CNBs and 180 repeated FNABs for thyroid nodules with initially non-diagnostic FNAB results were compared.<sup>15</sup> The incidence of non-diagnostic results for repeated FNAB was much higher than for CNB (40.0% vs 1.1%,  $p<0.001$ ). Furthermore, all statistical measures for the diagnosis of malignancy (including positive predictive value, negative predictive value, sensitivity, specificity and diagnostic accuracy) were higher for CNB. There were no complications in either of the two patient cohorts.

The largest series of CNBs to date was reported by Paja *et al*.<sup>16</sup> The authors retrospectively reviewed 676 thyroid nodules in patients who underwent surgery. CNB and pathological results were compared. There was only one major complication after direct puncture of the recurrent laryngeal nerve, causing permanent dysphonia. None of the minor complications (including 56 self-limiting haematomas) required treatment. The positive predictive value of CNB for malignancy was 98%. Paja *et al* concluded that CNB is safe, reliable and can be used as an alternative to FNAB as it demonstrated a low proportion of non-diagnostic and undetermined results, high sensitivity and a high positive predictive value.

Renshaw and Pinnar studied the results of 377 patients who underwent both FNAB and CNB for thyroid nodules.<sup>17</sup> The adequacy rate for CNB was significantly higher than that for FNAB (82.2% vs 70.3%,  $p<0.001$ ) although the combined adequacy (88.9%) was significantly higher than for either of the tests alone ( $p<0.001$ ).

The most important limitation of the study by Stangierski *et al* was the small number of cases (30 CNBs and 59 FNABs).<sup>18</sup> Their lack of statistically different results may also be related to the diameter of the needles. Their CNB needle was thin (22G), in contrast to the needles used by

Choi *et al* (18G),<sup>15</sup> Paja *et al* (18G),<sup>16</sup> and Renshaw and Pinnar (18–21G).<sup>17</sup> Acceptable larger needles for CNB in the study by Stangierski *et al* might have revealed statistically significant diagnostic differences.

For non-diagnostic FNAB results, current guidelines recommend repeated FNAB.<sup>13</sup> However, repeated FNABs have non-diagnostic rates of 17–47%.<sup>9–12</sup> CNB is a promising technique, with high accuracy and low non-diagnostic pathology results, especially for those cases with non-diagnostic FNAB. This can prevent delays in treatment due to non-diagnostic results for primary or secondary FNAB. It can also reduce the number of operations due to recurrent non-diagnostic FNABs.

### Limitations of core needle biopsy

There are some limitations of CNB when compared with FNAB. CNB cannot be performed on lesions measuring <1cm. Furthermore, CNB is more expensive than FNAB (\$20 vs \$2 at our institution). This is true even if a second FNAB has to be performed. In our experience, CNB is also a little more painful. Despite this, patients with initially non-diagnostic FNAB results were very satisfied with CNB owing to the reduction of anxiety caused by insufficient results.

CNB takes longer to perform than FNAB, especially during the learning curve (although this study did not measure the exact time). In addition, for the cases with initially non-diagnostic FNAB results from other centres, the level of experience of the radiologists and pathologists is not known. Experience is an important factor that could affect biopsy results.

### Conclusions

Our study comprised 1,000 CNBs (the largest series published to date) with 100% diagnostic accuracy and a 1.5% non-diagnostic rate. For cases with initially non-diagnostic FNAB results, our non-diagnostic rate was 0.7%. CNB is a safe and accurate method, and is more diagnostic than FNAB for nodular thyroid disease. We recommend CNB as an alternative to FNAB, especially for patients who have already had initially non-diagnostic FNAB results.

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