Prospective Evaluation of ThyroSPEC Molecular Testing of Indeterminate Thyroid Nodule Cytologies Following Diagnostic Pathway Optimization

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Introduction

- Thyroid nodules are highly prevalent and typically identified incidentally or from symptoms or palpation, which necessitates a clinical evaluation and ultrasound to assess malignancy risk.
- Quality ultrasound malignancy risk assessment allows rule-out of malignancy in ~50% of thyroid nodules, but historical local reporting was inadequate to risk stratify nodules according to guidelines.
- Suspicious nodules on ultrasound are referred to thyroid nodule fine needle aspiration cytology (FNAC), where malignancy is ruled out in another 60% of nodules. However, up to 30% of FNACs are indeterminate due to an inherent limitation of cytology with diagnostic surgery as the standard of care.
- Following evaluation of malignancy and resection rates across six S87.5 thyroid FNAC in Calgary, implementation of guidelines-based ultrasound reporting1, and implementation of a local thyroid nodule diagnostic pathway with the Calgary PCN2, we implemented reflexive ThyroSPEC™ testing in Calgary for indeterminate thyroid FNAC molecular diagnosis.
- In this ongoing study we examine the outcomes of implementing the above improvements in the local diagnostic pathway.

Cohort

- 439 consecutive patients with indeterminate thyroid FNAC collected from July 29, 2020, until December 31, 2021.
- 89% AUS/LUS (Bethesda III), 11% FN/SFN (Bethesda IV) on cytology.
- 104 patients underwent surgery by December 31, 2023.
- Median age of 54 years, 75% of patients were female.

Optimized Pathway

Following collaboration with local radiology practices, guidelines-based thyroid ultrasound malignancy risk stratification was recently implemented locally1.

The ultrasound score (report quality measured by the number of documented nodule features for each ultrasound) significantly improved (p<0.01) from historical levels, this means that guidelines-based ultrasound malignancy risk stratification is now available for clinical decision making alongside ThyroSPEC™ for nearly all indeterminate FNAC.

Thus, since implementation of reflex ThyroSPEC™ testing, mutation status is the predominant reason for surgery in ThyroSPEC™ positive reverted nodules which demonstrates a direct impact of ThyroSPEC™ on clinical decision-making.

Since implementation of reflex ThyroSPEC™ testing and optimization of the upstream components of the local thyroid nodule diagnostic pathway, unnecessary diagnostic procedures including FNAs and surgeries have been avoided while diagnostic yield has increased. Molecular diagnostics has provided accurate, incremental pre-surgical malignancy risk stratification, thereby improving referral patterns and surgical triage which directly benefits patients.

Conclusions

- Molecular data in the context of an optimized diagnostic pathway provides the following clinical benefits:
  - Improved surgical triage for FNAC with high risk mutations and a far higher rate of surgery in ThyroSPEC™ positive than negative nodules.
  - Genetic alterations identified by ThyroSPEC™ are the predominant reason for surgery in ThyroSPEC™ positive indeterminate FNAC, demonstrating direct impact of molecular diagnostics on clinical decision-making.
  - Reduced repeat FNAs, complete thyroidectomies, and total surgeries provide immediate reductions in patient morbidity resulting from overtreatment and represents cost savings achieved through a locally optimized thyroid nodule diagnostic pathway.
  - Despite fewer overall surgeries, more malignant nodules have been resected since ThyroSPEC™ implementation through a significantly improved diagnostic yield compared to historical cohorts.

Next Steps

- This study is ongoing to generate sufficient power for the analysis of subsets such as ThyroSPEC™ performance in intermediate suspicion ultrasound categories where decision making is most differential.
- We are working on multiple projects to improve the sensitivity of ThyroSPEC™ with the goal to improve sensitivity enough for ThyroSPEC™ to become a rule-out test, such that a negative (wild type) result could rule-out malignancy.
- We intend to create an integrated, clinically applicable regression classifier model that combines ultrasound, cytology, and molecular data to estimate a personalized risk of malignancy for each patient and provide a locally validated treatment algorithm.
- For more information, reach out to: contact@thyrospec.com

References

1. Stewardson, Paul; Eszllinger, Markus; Wu, Jiuhui; Khalil, Moosa; Cheung, Winnon; Box, Adrian; Paschke, Ralf: ThyroSPEC™ Molecular Testing of Indeterminate Thyroid Nodule Cytologies Following Diagnostic Pathway Optimization. University of Calgary, 2023.
2. Stewardson, Paul; Eszllinger, Markus; Wu, Jiuhui; Khalil, Moosa; Cheung, Winnon; Box, Adrian; Paschke, Ralf: ThyroSPEC™ Molecular Testing of Indeterminate Thyroid Nodule Cytologies Following Diagnostic Pathway Optimization. University of Calgary, 2023.
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5. Stewardson, Paul; Eszllinger, Markus; Wu, Jiuhui; Khalil, Moosa; Cheung, Winnon; Box, Adrian; Paschke, Ralf: ThyroSPEC™ Molecular Testing of Indeterminate Thyroid Nodule Cytologies Following Diagnostic Pathway Optimization. University of Calgary, 2023.