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CASE SERIES

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Using the GenCut core biopsy tool with the radial endobronchial ultrasound guide sheath enables a high-quality histology sample capable of programmed cell death ligand 1 (PD-L1) testing

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Abstract

Radial EndoBronchial UltraSound (R-EBUS)-guided biopsies are a promising biopsy technique for pulmonary nodules suspected of lung cancer with great safety profile. Programmed cell death ligand 1 (PD-L1) testing is increasingly demanded from lung biopsies. GenCut is a novel blunt tool that can be used to obtain core biopsies. This case series explores prospective performance of the GenCut core biopsy with R-EBUS. Once Peripheral Pulmonary Lesion was located, GenCut biopsy was performed followed by conventional (forceps ± cytology brush) R-EBUS biopsies. The overall diagnostic yield for the 16 patients with a mean peripheral pulmonary lesion (PPL) size of 4.1 cm was 100% from multi-modal R-EBUS sampling. The diagnostic yield for GenCut tool alone was 13/16 (81.2%) and the ability to perform PD-L1 from GenCut was 10/16 (62.5%). There were no adverse events recorded. GenCut tool is a novel blunt instrument that can be used safely to obtain a core biopsy suitable for PD-L1 in combination with R-EBUS without compromising the high safety profile.

KEYWORDS
GenCut core biopsy, lung cancer, PD-L1, radial EBUS, safety

INTRODUCTION

With the advancement of lung cancer treatment with novel immunotherapies, including programmed cell death ligand 1 (PD-L1), a core biopsy sample is preferred to make a diagnosis. Despite the increased safety of radial EBUS (R-EBUS), diagnostic yield is sub-optimal (74%)[1,2] and the ability to perform PD-L1 was not explored. The smaller size and crush artefacts from R-EBUS forceps[3] maybe overcome by the addition of cryobiopsy but requires expensive facilities[4–6] including general anaesthesia, fluoroscopy and additional measures to improve safety[5] (i.e., bronchial blockers ± rigid bronchoscopy for haemostasis). This study explores the ability of the novel GenCut biopsy to obtain a histology sample suitable for PD-L1 testing under sedation.

METHODS/DESCRIPTION

This is a prospective, interventional, pilot case series performed at two tertiary hospitals in Australia from February 2018 to January 2019 (Ethics approval: AU RED HREC/17/WMEAD/461 and trial registration number: ANCTR-U1111-1204-2333). The co-primary end points were the ability to obtain a histology sample suitable for PDL-1 from GenCut biopsy (Medtronic Pty Ltd) and the safety of the procedure.

All patients referred to R-EBUS were offered GenCut in addition to at least one conventional R-EBUS biopsy (forceps, brush and needle aspiration). Lesions >1.5 cm in size, located in the outer half of the lung parenchyma, were included. Patients unsuitable for flexible bronchoscopy were excluded. The procedure was performed in endoscopy suit in accordance with the institutional guidelines. The R-EBUS ultrasound (USS) probe (20 MHz, UM-BS20-20R, Olympus, Tokyo, Japan) was used within the large guide sheath (GS) (Olympus K-203). The GenCut was introduced through the GS as the first mode of biopsy, followed by conventional R-EBUS biopsies.

GenCut (Covidien-GenCut-core-biopsy-system) had demonstrated satisfactory histology samples in porcine models.[7] It is a flexible (1140 mm length, 1.9 mm diameter) hollow tube with a 1-cm blunt metal tip comprising of inwardly placed sharp blades (Figure 1). Once in the lesion, suction is applied using a lockable 20-ml syringe. The suction ensures that the tumour is 'anchored' into the biopsy tool. The tool was then rotated clockwise 45° at a time, whilst maintaining the suction, to complete a 360° rotation, ensuring ongoing acquisition of material via suction into the tool (Figure 1). The specimen was pushed out using air via a 10-ml syringe to Hanks's solution, followed by a cytology brush insertion and a 10-ml saline push to expel the residual tissue. Samples were then placed in formalin.

Suitability of PD-L1 testing was assessed by an independent pathologist from each institution for all samples and documented in a standardized format. The procedures were performed in the endoscopy suit with either sedation alone or with general anaesthesia and with laryngeal mask airway. A chest x-ray was performed 1-h post-procedure. Fluoroscopy was used if the proceduralist requested it. Routine follow-up was executed. Data collection forms for patient demography, adverse events, pathology sampling and bronchoscopy were completed.

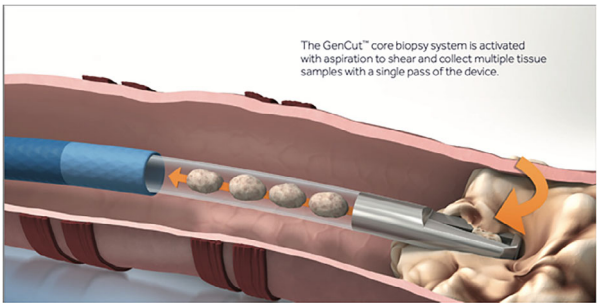

FIGURE 1 GenCut core biopsy tool demonstrating 'anchoring' to the tissue via suction and the samples drawn into the tool (courtesy of Medtronic's Pty Ltd)

RESULTS

Eighteen patients were recruited during the study period: nine males (50%), mean age 67 years (SD 11.8). Thirteen (72%) were current or ex-smokers. Seven of 18 (35%) had chronic obstructive airways disease, 5/18 (27%) had cardiac disease and 3/18 (16%) had type 2 diabetes mellitus. No one recorded pulmonary hypertension.

The mean lesion size was 4.1 cm (SD 1.3 cm). Eight were in the left upper lobe (LUL), seven in the right upper lobe (RUL) and three in lower lobes. Eleven of 18 (61%) had sedation and seven had general anaesthesia for the procedure. Two of 18 did not proceed with the study; one had resolution of peripheral pulmonary lesion (PPL) confirmed on chest computed tomography and one had a positive paratracheal lymph node on linear EBUS.

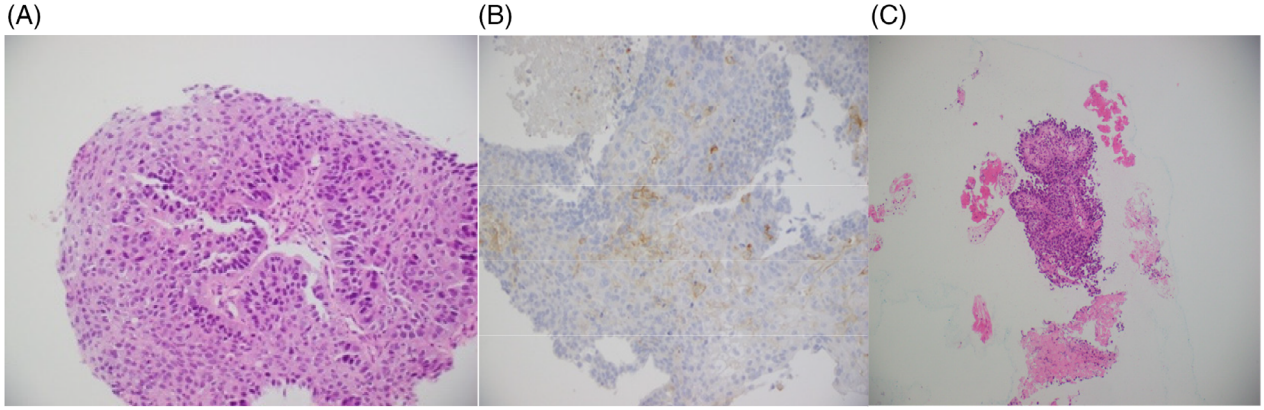

FIGURE 2 Well-preserved histology sample of a GenCut biopsy demonstrating squamous cell carcinoma, haematoxylin and eosin (H&E) staining ×20 (A) and weak programmed cell death ligand 1 (PD-L1) staining 8% of the same core biopsy sample (B), compared to forceps biopsy with H&E staining ×20 (C)

Sixteen completed the R-EBUS. Fifteen (93%) had a concentric USS visibility. The mean procedure time was 41 min (SD 13.9 min). The mean time to detect the lesion was 1.47 min (SD 1.5 min). Fluoroscopy was used for 9/16 (53%). The anaesthetic agents used and mean values were 1% lignocaine (14 mL, SD 4.9 mL), midazolam (3.6 mg, SD 1.9 mg), fentanyl (85 mcg, SD 20.8 mcg) and propofol (50 mcg, SD 57.9 mcg).

All 16/16 (100%) had a successful diagnosis made from combined R-EBUS sampling. GenCut was not performed for 2/16 due to technical difficulties. One had excessive secretions and difficulty in accessing the RUL, and one had a highly friable mucosa in the LUL and the GenCut tool could not be 'anchored' to the airway to obtain adequate suction to draw the tissue into the tool. Both these PPL were diagnosed using a cytology brush and forceps biopsy, respectively.

The overall diagnostic yield from GenCut alone was 13/16 (81.2%) and the ability to perform PD-L1 from GenCut alone was 76% (10/13). Overall diagnostic yield from forceps biopsy alone was 75% (12/16) with 8/12 (66%) suitable for PD-L1 testing. However, in samples where both GenCut and forceps biopsies were suitable for PD-L1 testing, PD-L1 testing was performed using the GenCut core biopsy due to the preserved architecture (Figure 2A,B) in comparison to radial forceps (Figure 2C). The mean biopsy size of GenCut was 6.8 mm (2–18 mm) and forceps biopsy was 2.8 mm (1–7 mm).

Four of 13 had a single pass and 9/13 had two passes with GenCut. Other R-EBUS instruments used and the median number of passes were radial forceps ($n = 14$, mean 3.6, median 3), radial brush ($n = 11$, mean 1.5, median 2) and aspiration needle ($n = 5$, mean 1.4, median 2). There were 18 malignant PPL (66% adenocarcinoma, 33% squamous cell carcinoma) and two benign PPL (type 2 pneumocyte hyperplasia, eosinophilic hyperplasia).

There were no pneumothorax, pulmonary haemorrhage or unexpected representation to the hospital. All patients were discharged as planned.

DISCUSSION

Our study demonstrates that the ability of GenCut biopsy to make a diagnosis and perform PD-L1 was high. Despite the large sample sizes, there were no adverse events.

Compared to cryobiopsy for PPL, which requires rigid bronchoscopy, bronchial blockers and anaesthetic support to obtain a core biopsy, GenCut does not require extra equipment apart from the GenCut tool and it is logistically easy to incorporate into any unit that has R-EBUS services. The procedure can be performed with sedation in endoscopy suite. Fluoroscopy was not essential, although it may be more helpful in smaller and eccentric lesions. Accurate instrument measurement with the GS prior to the procedure is mandatory to obtain excellent results.

GenCut is used in a similar manner to conventional radial instruments. The tool easily slides into the large GS of the R-EBUS. It is flexible and bends upon itself enabling easy access to upper lobes. The study lesions were in the outer half of the lung and GenCut can be used in small tapering airways.

Few studies had demonstrated the ability of small R-EBUS samples to obtain satisfactory PD-L1 testing[8]; however, the published literature on GenCut core biopsy is sparse. A procaine model study demonstrated better samples with GenCut core biopsy compared to transbronchial biopsies.[7] In a recent publication by Lea et al.[9] on using GenCut tool and transbronchial biopsies in 324 lung nodules, GenCut tool had a diagnostic yield of 37.3% and transbronchial biopsy had a diagnostic yield of 43.2%. However, when PPL > 3 cm was analysed separately, the diagnostic yield was 65.2% with both GenCut and transbronchial biopsy. In our study, the diagnostic yield may have been higher due to the large mean size of the PPL in comparison to Orr et al. They used R-EBUS in 96% of patients and electromagnetic navigation (EMN) bronchoscopy in 49%. EMN was used in more peripheral PPL. In our study, all PPL were in the outer half of the lung parenchyma and did not require the EMN, which may be again due to the larger mean size of the PPL in our study.

The main limitation of the study is the inclusion of only larger lesion size (>1.5). Smaller lesions are not represented here in efficacy or safety. 'Anchoring' to the lesion was not successful in all lesions and using GenCut as the sole biopsy method is not encouraged. The small sample size of this series is another limitation. Other molecular testing including EGFR and ROS1 were not analysed during this study.

In conclusion, the novel GenCut biopsy with R-EBUS via the large GS is successful in obtaining a histology sample suitable for PD-L1. GenCut can be used without additional equipment, safely with sedation and is applicable to most centres.

CONFLICT OF INTEREST

None declared.

No financial disclosures for all authors. There were no commercial interest or trial subsidies offered for this study.

AUTHOR CONTRIBUTION

Dr Samantha Herath had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis, including and especially any adverse effects. Dr Samantha Herath, Dr Farzad Bashirzadeh, Dr Hema Mahajan, Prof. Alvin Ing and A/Prof David Fielding contributed substantially to the study design, data analysis and interpretation, and the writing of the manuscript.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

This study was approved with ethics approval: AU RED HREC/17/WMEAD/461 and trial registration number: ANCTR-U1111-1204-2333.

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