

THE "POOR MAN'S CELL-BLOCK" SAMPLE PREPARATION METHOD FOR EUS-FNA OF MEDIASTINAL AND RETROPERITONEAL LESIONS DOES NOT REQUIRE ATTENDING PATHOLOGY STAFF OR CYTOLOGY EXPERTISE



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INTRODUCTION

We present a novel technique of sample preparation for endoscopic ultrasound (EUS) that is simple, convenient and yields a high diagnostic rate. EUS-guided fine needle aspirate (FNA) is increasingly used to obtain tissue in the mediastinum and retroperitoneum. Compared with surgical biopsy, EUS is minimally invasive and safe. The procedure, however is not without risk and it is therefore imperative that sampled tissue is optimally prepared. Ideally sample preparation should be simple without the need for an attending pathologist, and enable specific diagnosis and prognostics. The novel "poor man's cell block"¹ (PMCB) technique, recently adopted in our institution for all EUS FNA, fulfils this need. The PMCB technique allows the entire sample to be processed "as a biopsy". No special equipment or slide preparation skills are needed, and pathology staff need not be present. Resultant H&E stained slides can be reported without specific training in cytopathology. PMCBs facilitate additional studies such as immunohistochemistry to enable subclassification and risk stratification of certain neoplasms.

MATERIALS AND METHODS

All samples were taken by a radiologist (BF) using an "EchoTip ProCore 19/22 gauge needle, and reported by a histocytopathologist (TB). All mediastinal and retroperitoneal (mostly pancreatic) cytology and histology samples were retrospectively retrieved from the pathology database, since the authors began performing EUS FNA using the PMCB technique (2012-2013). The PMCB technique was carried out as previously described by Mayall and Darlington¹. Additional passes were carried out to prepare Pap-stained conventional cytology slides in parallel with most of the PMCB preparations. On site evaluation of cytology preparations by pathology staff was not routinely available at the time of the study.

For simplicity of interpretation and presentation of results the following scheme was used for cytology (C) and PMCB (PM) results;

C/PM1= insufficient for diagnosis, C/PM2= benign, C/PM3= probably benign, C/PM4= probably malignant, C/PM5= malignant / definite tumour

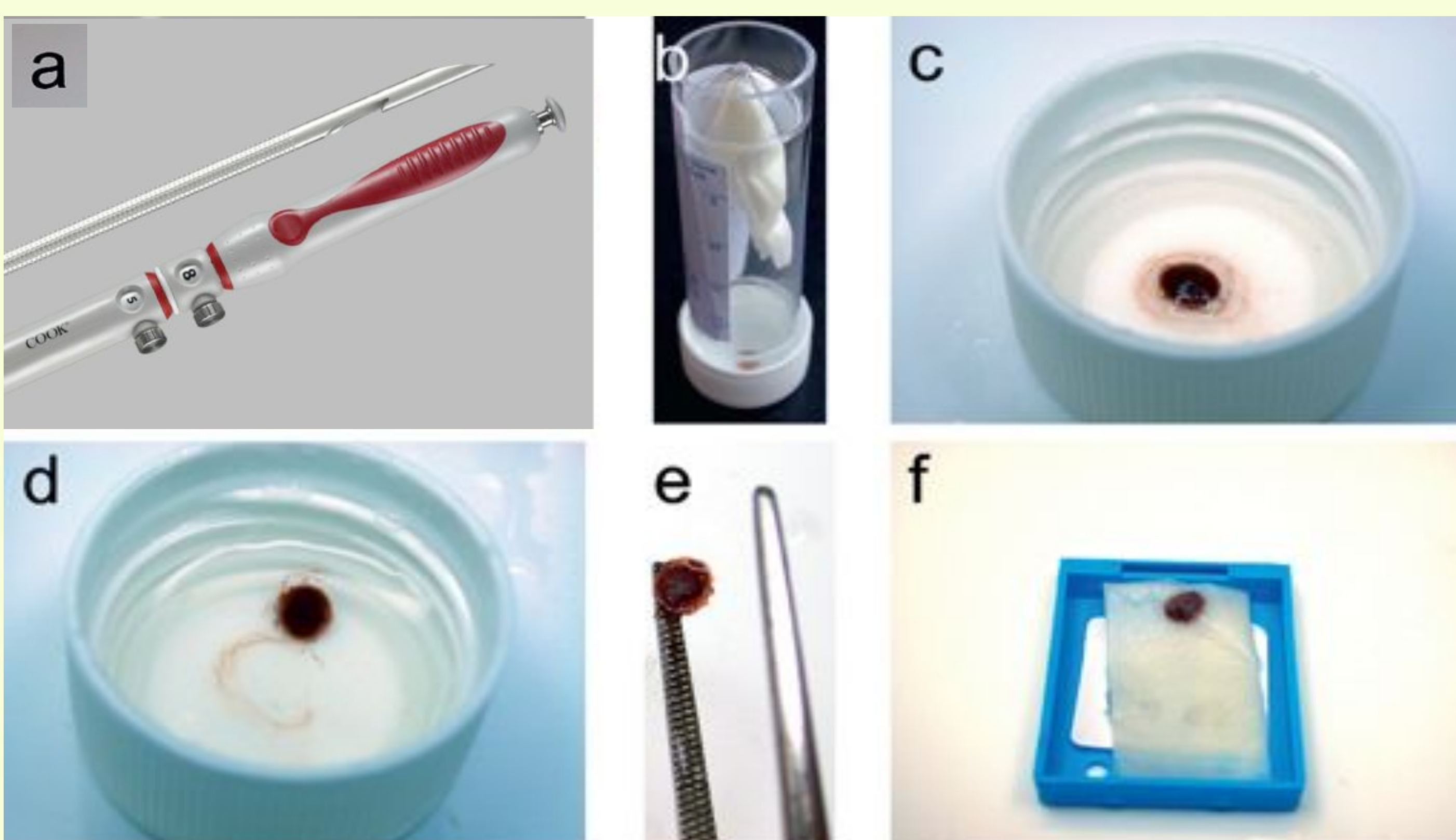


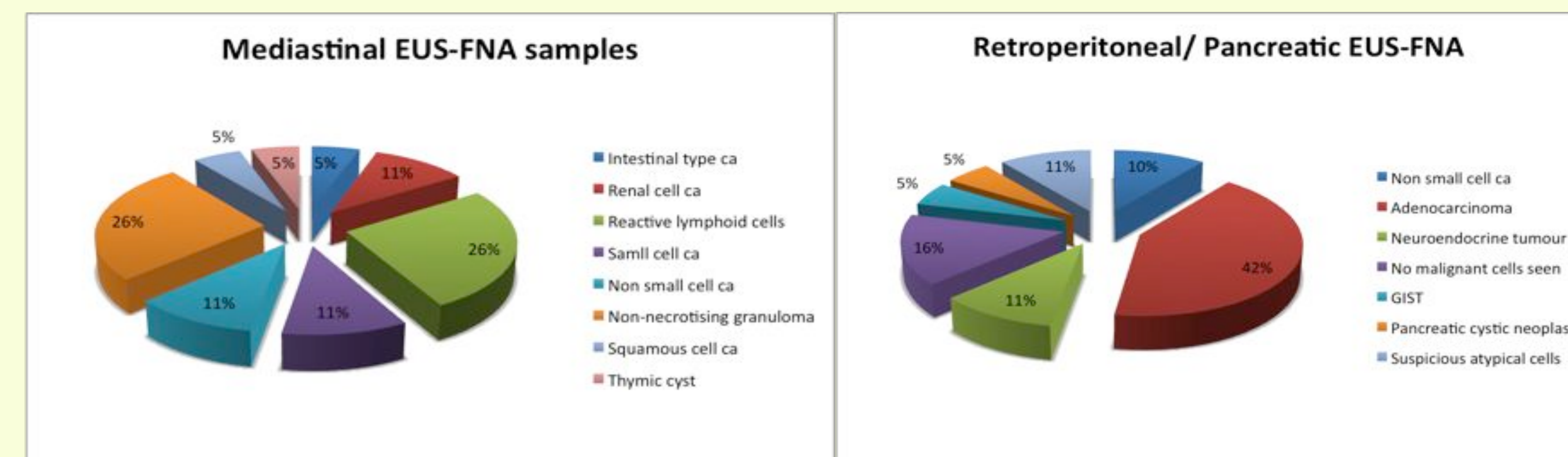
FIGURE 1. a= EchoTip ProCore 19/22 gauge needle, b-f= PMCB technique showing formalin soaked gauze in base of inverted universal lid (b), when fixed can be displaced using forceps, manipulated (d, e) and processed "like a biopsy" (f).

RESULTS

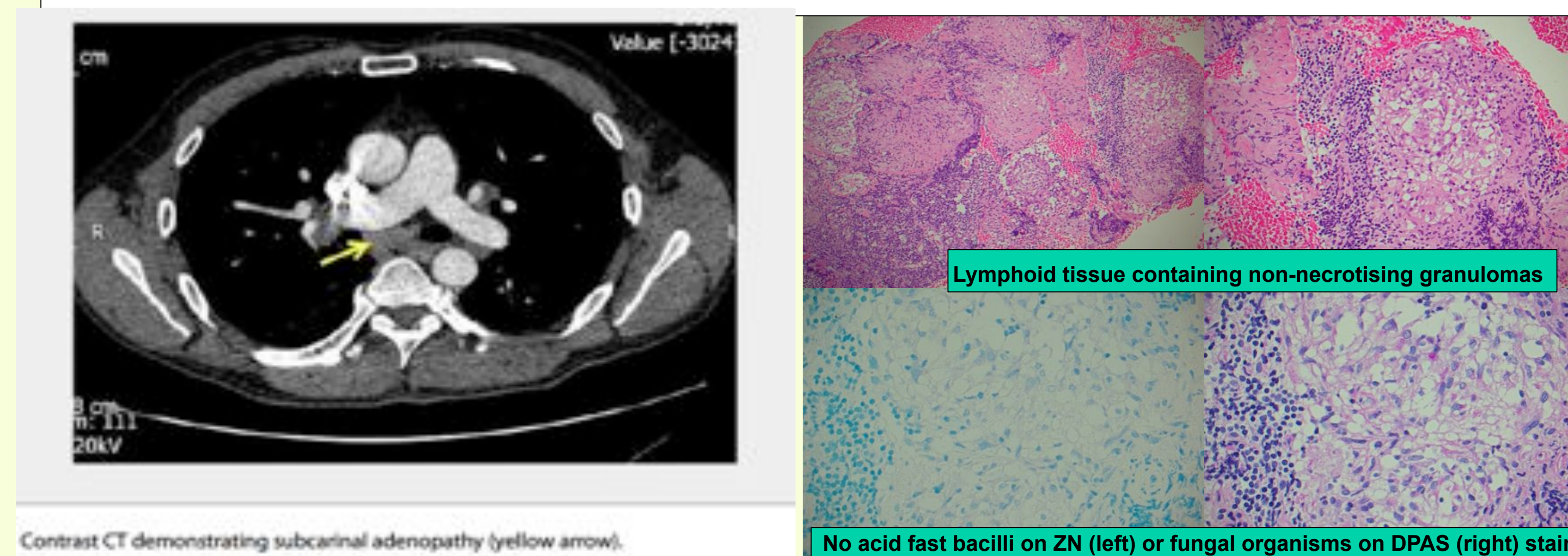
A total of 69 cases were analysed (36 retroperitoneal, 33 mediastinal; at least half of each were received with paired cytology samples). The table below demonstrates that the overall diagnostic rate was 61% and that the PMCB technique gave a higher diagnostic rate for both mediastinal (100%) and retroperitoneal (78%) samples. For the diagnostic cases in both anatomical sites approximately 60% were tumour/malignant, the mediastinal samples frequently showed granulomas consistent with a benign diagnosis. Most cases where cytology was sent in parallel with the PMCB, showed a good correlation between benign and malignant diagnoses. There were, however 2 retroperitoneal and 1 mediastinal "false negative" cytology samples proven to be malignant on the PMCB sent in parallel. In addition, the PMCB afforded more specific malignant diagnoses, and tumours of uncertain malignant potential (eg. GIST / neuroendocrine neoplasms) could be approximately graded and risk stratified (aided by immunohistochemistry). Since this pilot study Hodgkin and non-Hodgkin lymphomas have also been diagnosed using the PMCB technique. There was no increase in turnaround time for PCMB reports compared with other departmental biopsies and cytology.

	Cytology	PMCB
Overall - 61%	67%	78%
Mediastinal	80%	100%
Retroperitoneal	57%	63%

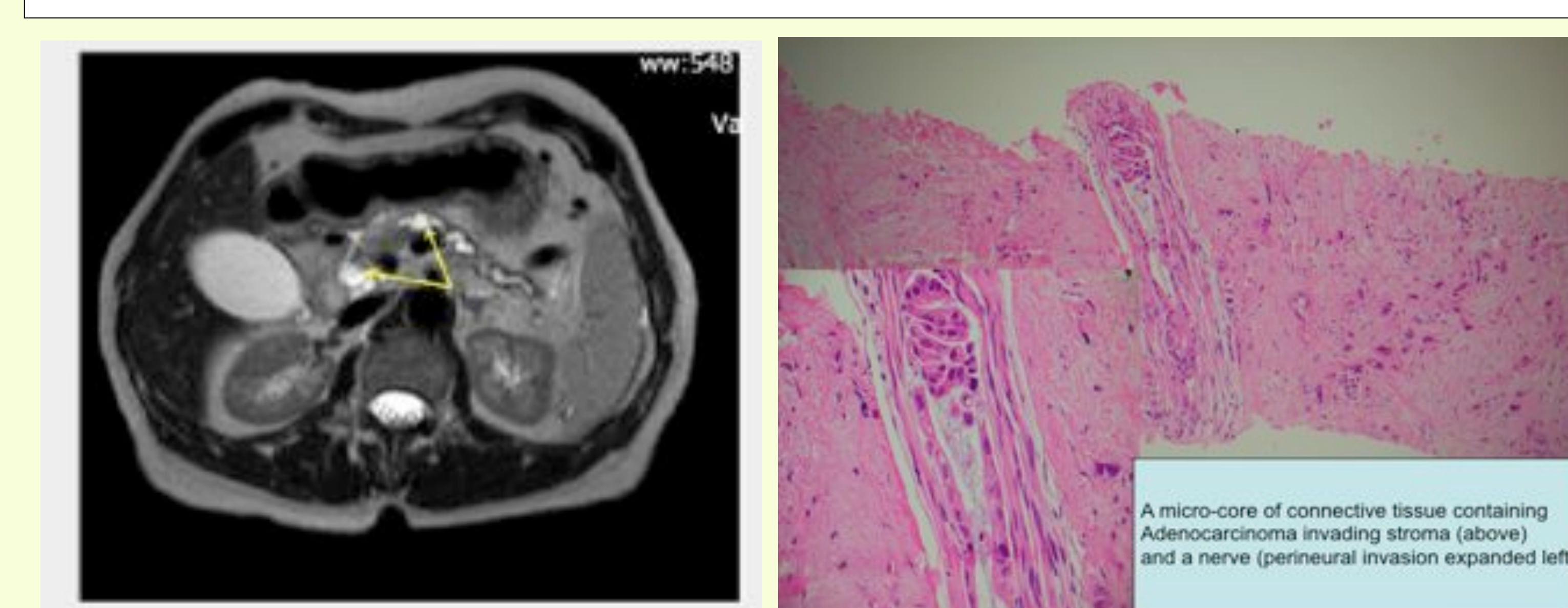
Table 1: Comparison of adequacy rates between cytology and PMCB samples



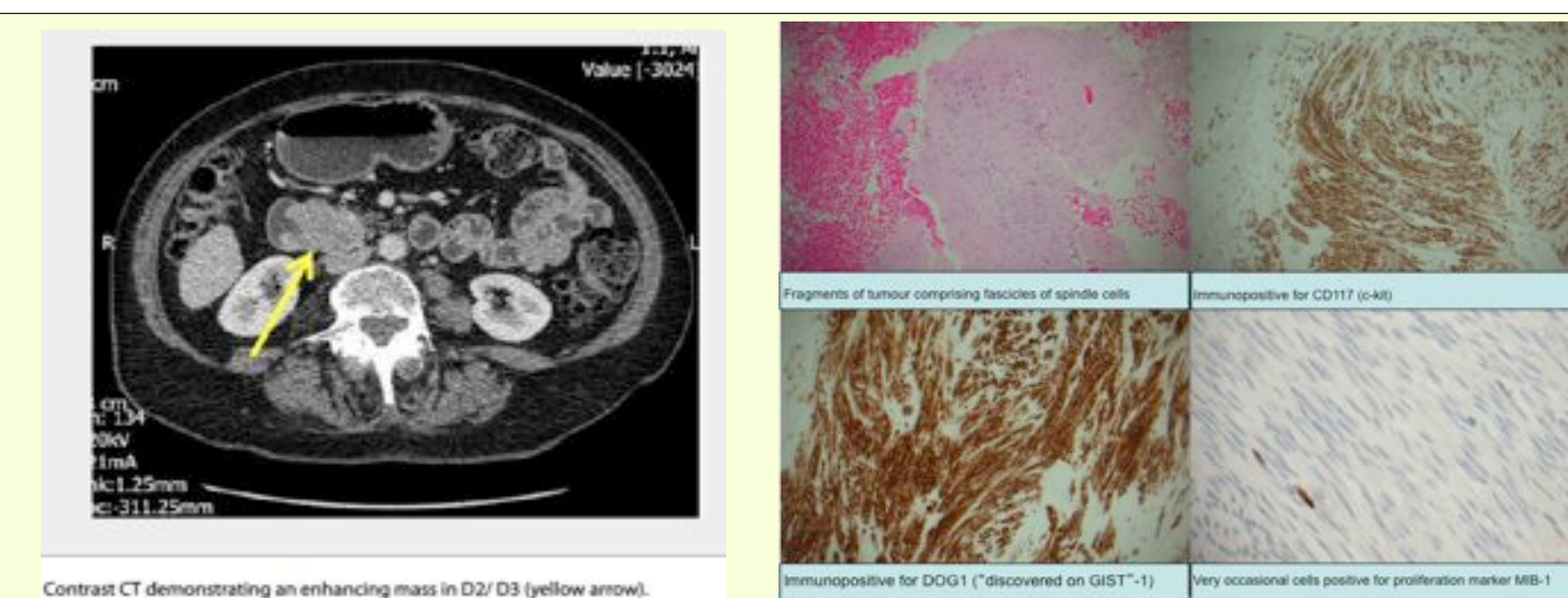
EXAMPLE CASE 1 – 44yo male mediastinal lymphadenopathy = sarcoidosis



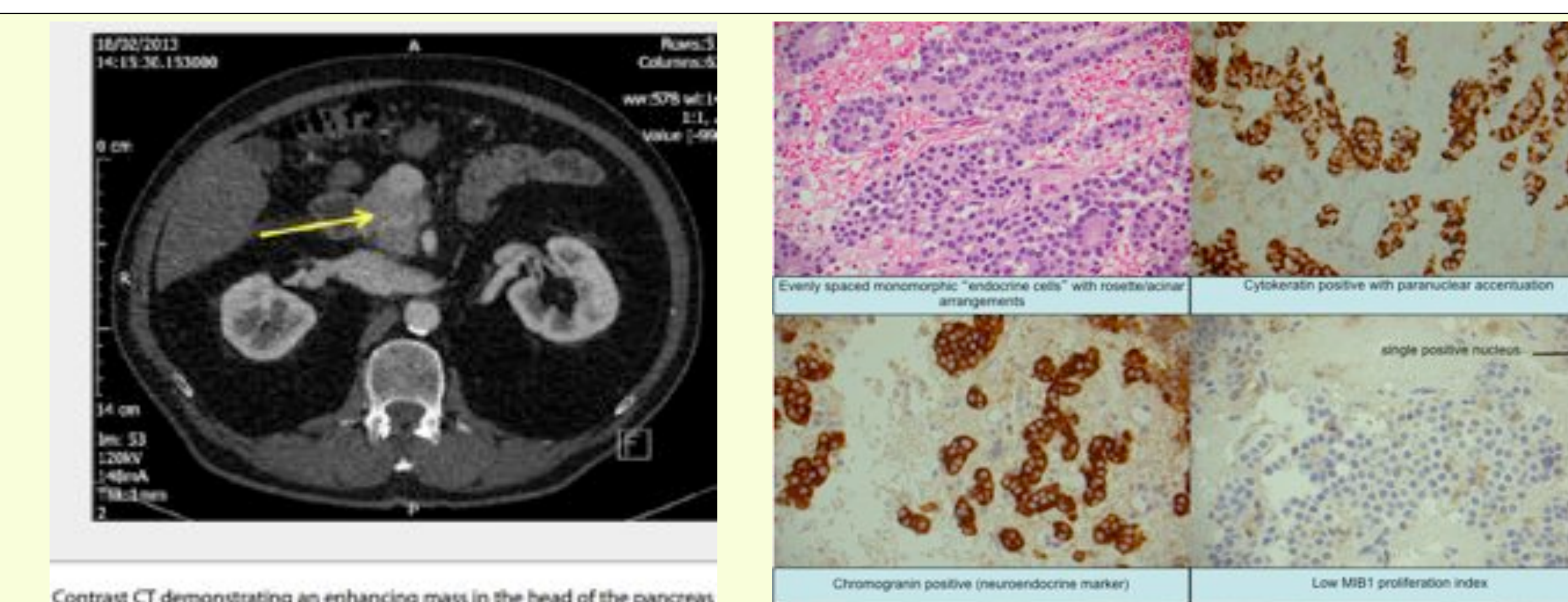
EXAMPLE CASE 2 – 63 yo female pancreatic mass = adenocarcinoma with nerve invasion



EXAMPLE CASE 3 – 70yo female D2/D3 mass = spindle cell GIST



EXAMPLE CASE 4 – 80yo male, polycythaemia pancreatic mass = well diff NET



DISCUSSION AND CONCLUSIONS

EUS FNA is increasingly used to sample lesions in anatomical locations difficult to access by other non-invasive methods. Adequacy rates vary widely in the literature and many consider ROSE (rapid on site evaluation) of cytology preparations to be the "gold standard" in the diagnosis of mediastinal and retroperitoneal lesions. In ROSE, a cytologist/cytotechnician prepares and examines aspirated material immediately to determine if a diagnosis can be made. Depending on the provisional diagnosis, additional passes can be made by the EUS practitioner and the material can be prepared according to the pathology encountered. Increasingly there is a trend towards a national shortage of pathologists, and fewer pathologists are trained in cytopathology. With increasing pressure on pathologists, fewer centres are able to offer pathology support for ROSE.

In the absence of ROSE, there is arguably little value in producing cytology preparations in addition to cell blocks, as although cytology is sensitive in the diagnosis of malignancy, it lacks specificity² and does not facilitate immunological subtyping. Unlike histology, cytology cannot distinguish pre-invasive and invasive neoplasia. In the authors' experience, the "poor man's cell block" (PMCB) is superior to cytology, and offers advantages over traditional cell block preparations, particularly for EUS samples. EUS material is more voluminous and viscous than traditional percutaneous FNA samples. Worm-like coils and micro-fragments are often yielded by the larger cutting needle and the lesional material is often "contaminated" by non-lesional gastrointestinal mucosa "picked up en route". In traditional cytology preparations viscous material and microbiopsy fragments are difficult to spread and visualise; non-lesional mucosa is often mixed with the lesional cells making interpretation very difficult. Our experience with the PMCB is that lesional and non-lesional material is spatially separated on sections and very easily distinguished. There is no need to mix or centrifuge the sample and the architecture is retained in the microbiopsy fragments. In some cases (see example case 2) stromal and perineural invasion can be demonstrated, enabling specific and confident diagnoses. Since the entire sample is available in a wax block, further stains and prognostic markers can be easily applied pre-diagnosis or later.

In conclusion the PMCB technique is a simple, reliable and cost-effective EUS-FNA sample preparation technique that in our hands appears superior to conventional cytology preparations. PMCB can potentially be reported by any histopathologist, without additional cytology training or expertise. PMCB allows more accurate diagnosis with the additional benefit that all the aspirated material is subsequently available for further analysis, predictive biomarkers, and risk stratification for some neoplasms.

References

- Mayall, F. & Darlington, A. (2010) The poor man's cell block. *J Clin Path* 63: 837-838.
- Kopelman Y et al., (2011) Value of EUS-FNA cytological preparations compared with cell block sections. *Cytopathology*. 22:174-8.