

# Retrospective evaluation of endoscopic and histological handling of colorectal biopsies on sample adequacy for molecular testing

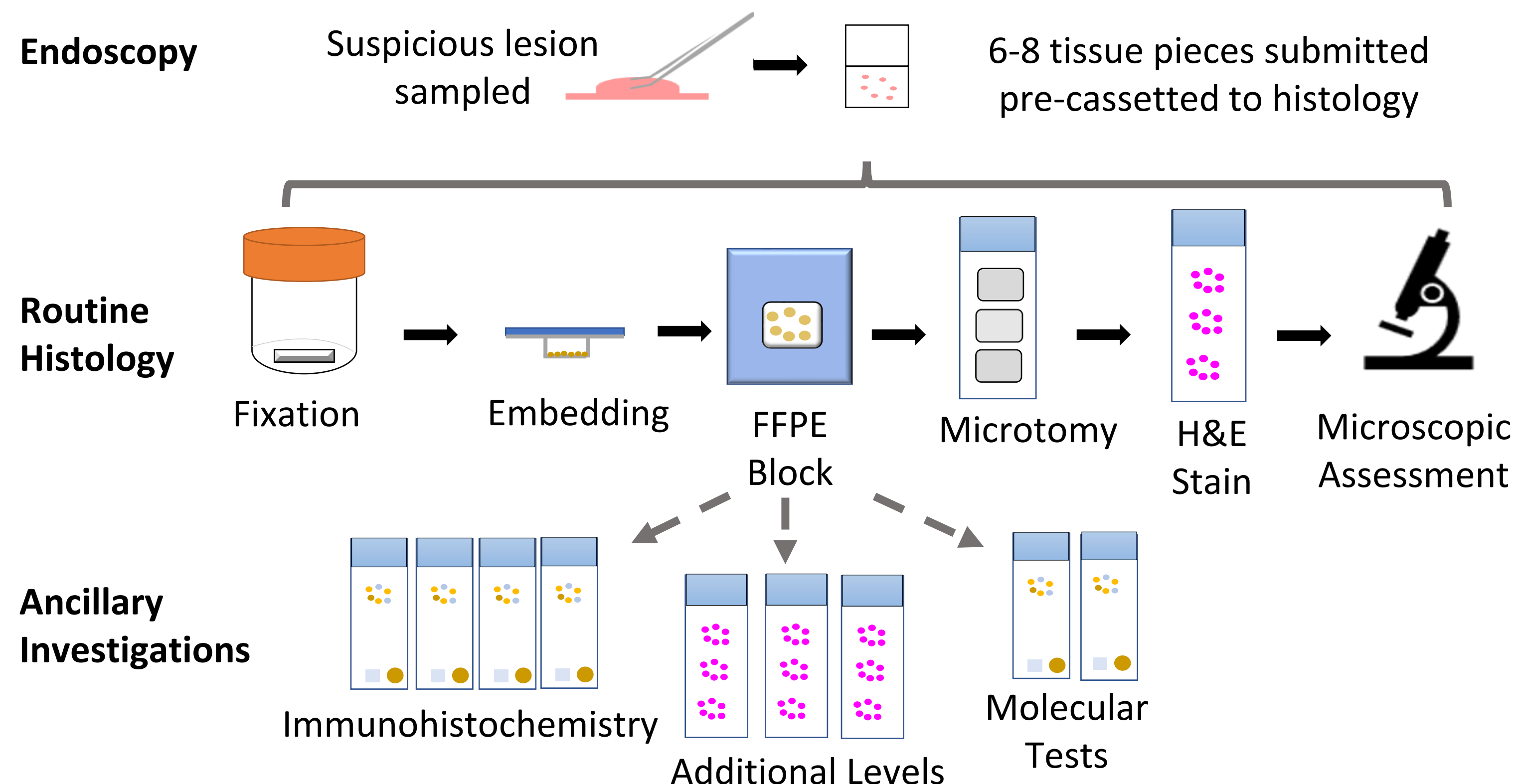
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## Introduction

Colorectal cancer (CRC) is the collective disease name for cancers arising from the colon and the rectum. In the UK, CRC has the second highest mortality rate of all cancer types emphasising the requirement for early detection and efficacious management. Local protocols recommend that a minimum of 6-8 tissue pieces should be sampled endoscopically from lesions suspicious for CRC, then submitted for histological diagnosis. Cancerous or suspicious lesions may require molecular testing to determine patient suitability for targeted treatment. Eligibility for molecular testing is subject to available pathology material; sample requirements are  $\geq 30\%$  neoplastic cell content or suitability for macrodissection. Concerns of colorectal biopsy ineligibility for molecular testing at Whiston Hospital demands retrospective clinical audit of local endoscopic and histological processes to enable service improvement.



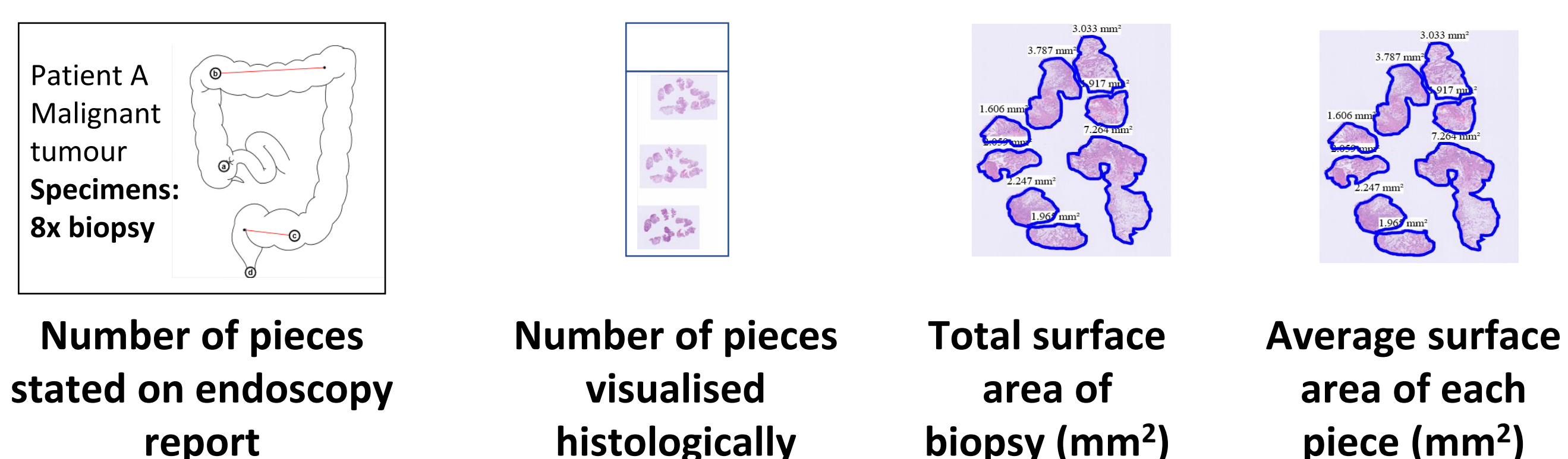
**Figure 1:** Endoscopic sampling of suspicious colorectal lesions and subsequent histology investigations. Ancillary investigations differ for each case, number of slides indicated in Figure 1 are used for demonstrative purposes only.

## Aims

- Evaluate adherence to local endoscopy protocols for suspicious colorectal lesions and identify trends between endoscopist performance and sample adequacy for molecular testing
- Determine the impact of histopathologists' primary diagnostic investigations on the adequacy of a sample for molecular testing
- Evaluate consistency between number of pieces obtained endoscopically and number of pieces evaluated histologically

## Methods

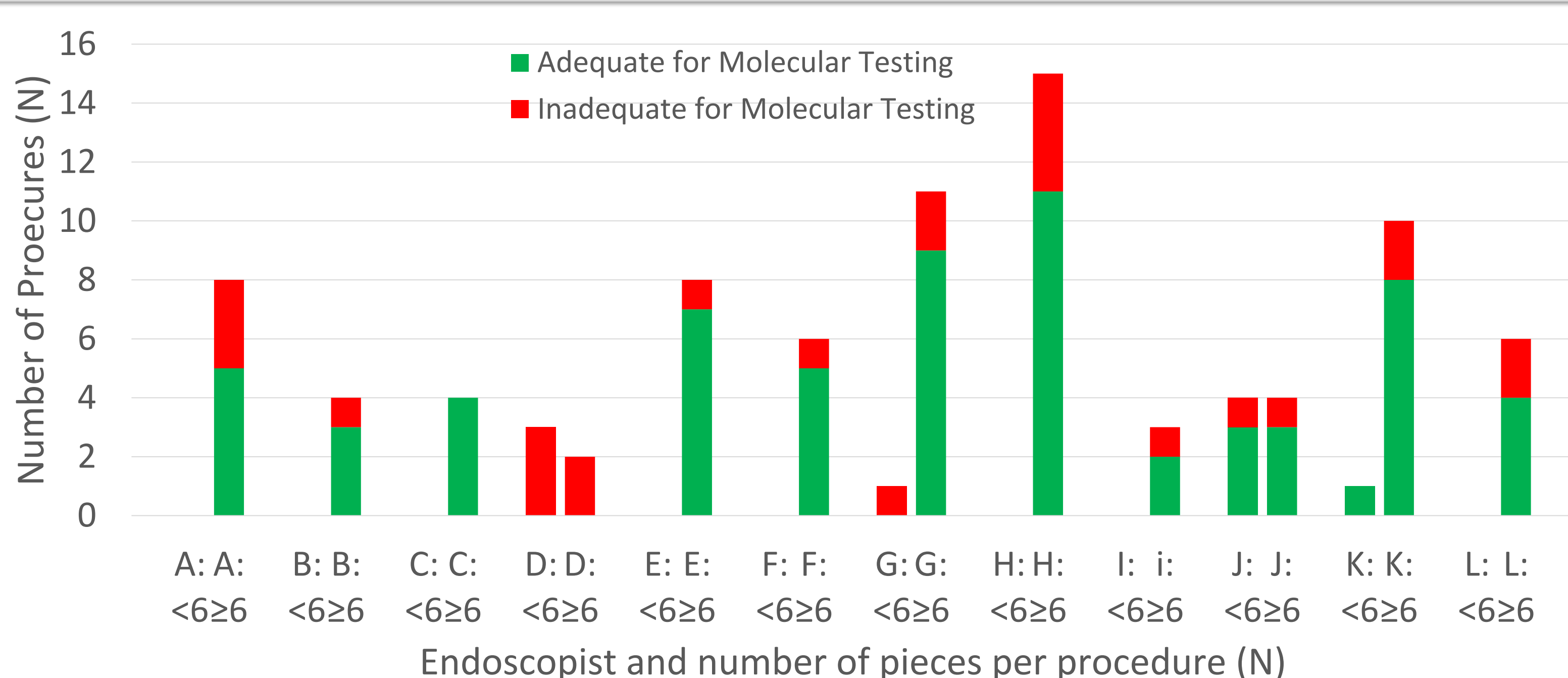
107 colorectal biopsies collected by 12 endoscopists from suspicious lesions were submitted for histological evaluation. 93 of which were treated as cancer so were evaluated with respect to adequacy for molecular testing. Four separate measurement techniques were used to evaluate amount of pathology material available for molecular testing. Blind re-assessment histologically was used to evaluate suitability of ancillary tests and to calculate neoplastic cell content.



**Figure 2:** Methods used to measure endoscopically obtained material

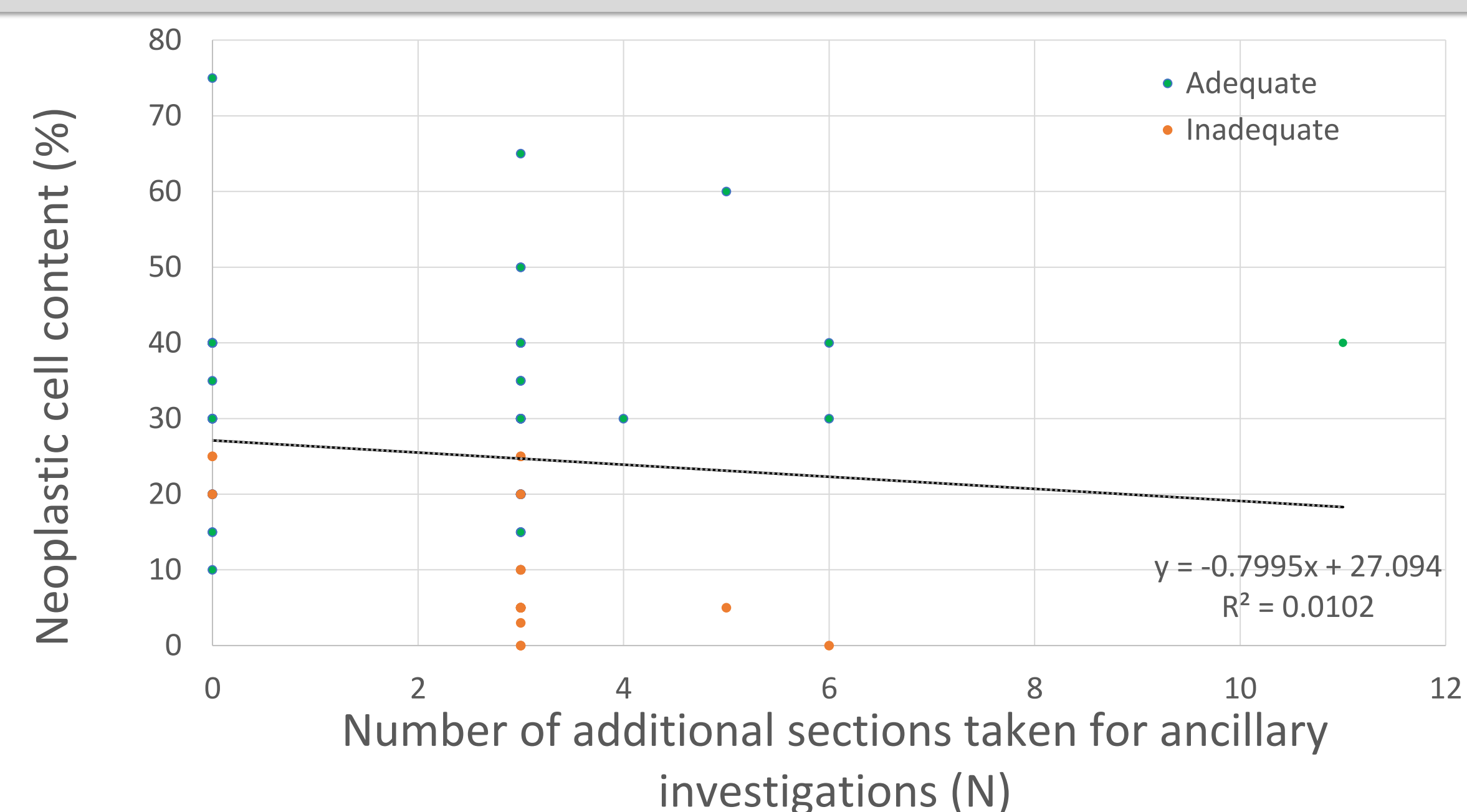
## Results

1. Local adherence to endoscopy sampling guidelines for suspicious colorectal lesions was 90% ( $n=83/92$ ). 92% of endoscopists consistently practiced within local guidelines obtaining a minimum of six tissue pieces per suspicious lesion. Adequacy for molecular testing is dependent on the number of pieces obtained at endoscopy ( $\chi^2(1)=4.061$ ,  $P=0.044$ ).



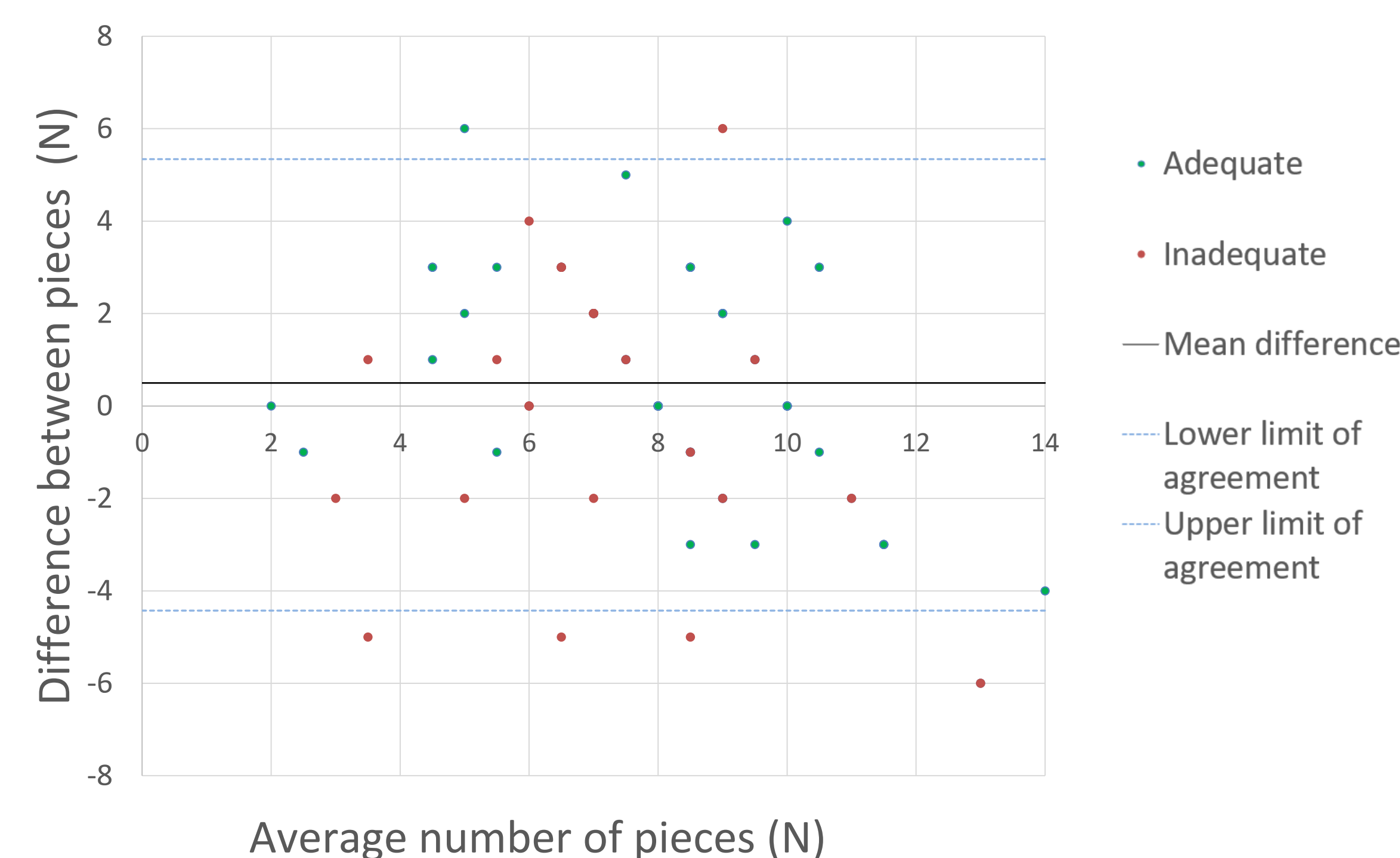
**Figure 3:** Number of tissue pieces obtained from suspicious lesions per endoscopist categorised by adherence to recommended guidelines (<6 or ≥6), with corresponding adequacy/inadequacy for downstream molecular tests.

2. 91% of ancillary histology investigations were considered necessary for primary diagnosis ( $n=60/66$ ). A weak, non-significant correlation was identified between additional sections for ancillary tests and neoplastic cell content ( $r=-0.101$ ,  $P=0.350$ ). Adequacy for molecular testing depends on number of ancillary investigations performed histologically ( $\chi^2(2)=5.692$ ,  $P=0.017$ ).

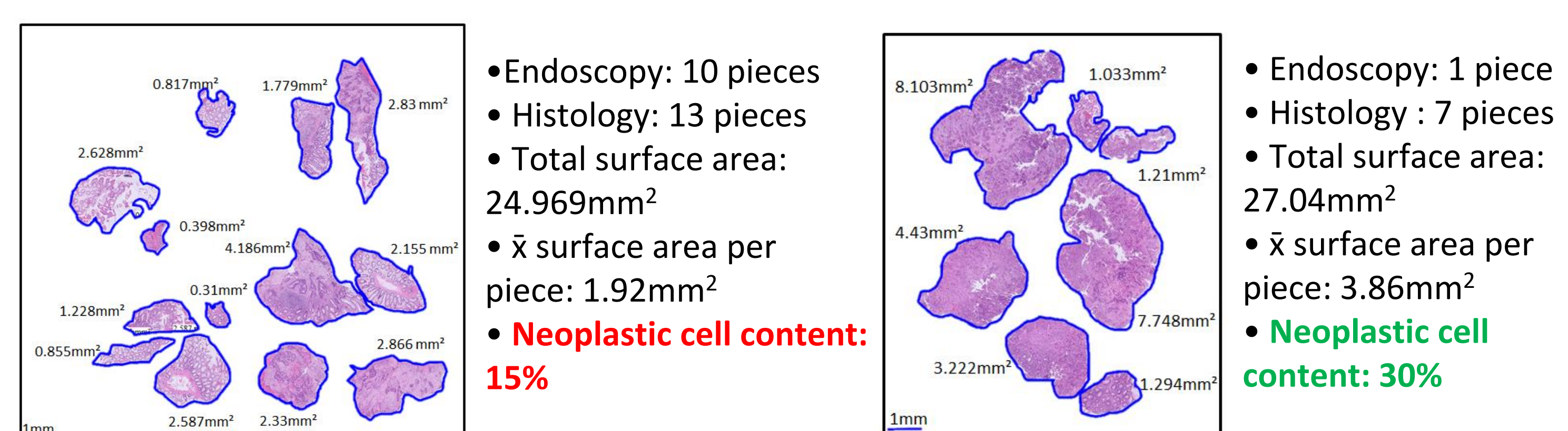


**Figure 4:** Relationship between number of ancillary investigations and neoplastic cell content (%)

3. Inconsistencies exist between number of pieces obtained endoscopically then evaluated histologically. Weak, non-significant correlations were identified between both the total surface area of the biopsy tissue, and the mean surface area per piece with respect to adequacy for molecular testing ( $r=0.068$ ,  $P=0.518$  and  $r=-0.081$ ,  $P=0.443$ , respectively).



**Figure 5:** Bland-Altman plot for limit of agreement between pieces obtained at endoscopy and pieces evaluated histologically.



**Figure 6:** 0.5x magnification. Demonstration of variations in all four measurements of endoscopically obtained material and corresponding neoplastic cell content.

## Conclusion

- Endoscopists mostly adhere to local protocols for suspicious colorectal lesions.
- Endoscopists that consistently obtain  $\geq 6$  tissue pieces from suspicious lesions produce higher numbers of samples adequate for molecular testing.
- Ancillary tests are mostly necessary; histopathologists that requested higher numbers of ancillary tests typically had a lower proportion of samples adequate for molecular testing.
- Number of pieces obtained at endoscopy is not always consistent with number of pieces assessed histologically.
- Tissue surface area does not always correlate to sample adequacy for molecular testing.
- Further work should consider the effects of recent changes to sample requirements (neoplastic cell content  $\geq 20\%$ ) on sample adequacy for molecular testing.

## References and Acknowledgements

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