



# A Comparison of Single Bite and Double Bite Biopsy Techniques in Gastrointestinal Endoscopy: A Scoping Review

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## Abstract

Endoscopic biopsies may be taken as single or double bite. In the former method intubation time may be proportionately prolonged depending upon the number of biopsies. In contrast to this, in the latter approach, although, a greater number of biopsies may be taken per unit time, equally, it may have effect on the quality of the biopsy specimen. This is because there is a perception that taking biopsies in such a manner may lead to crush artifacts and difficulty with orientation of the specimens. This, as a result, may pose diagnostic challenge to the histopathologist. A literature search was performed, and 11 studies, examining the histological quality of biopsies taken by these techniques, were identified. There were conflicting results. This is because there are considerable differences in the methodology, study power and interpretation of these studies. A holistic study is needed, which is clinically relevant, minimises selection bias and has sufficient power to clarify conflicting issues.

## Keywords

Biopsies, Endoscopy, Single bite, Double bite

## Introduction

Specimen collection is a routine procedure during endoscopy for the diagnosis and surveillance of various conditions. Furthermore, it is considered as gold standard and, at times, histopathological examination may be the only clue to the diagnosis of certain conditions such as microscopic colitis [1]. Moreover, both endoscopic and histologic diagnostic foci may be patchy; hence, multiple samples are recommended [2]. Similarly, in surveillance of chronic conditions i.e. Barrett's oesophagus, the number of biopsies taken may range from four to 40, depending on the length of the segment [3].

Biopsy samples which include mucosa and sub mucosa [1] and slides providing orientated mucosal tissue in a perpendicular plane demonstrating the entire layer of mucosa, from the mucosal surface to the Muscularis mucosa, may affect the diagnostic yield [3]. This is why histopathological examination requires meticulous handling and proper orientation of specimens i.e. to avoid tangential or horizontal sectioning [4]. An endoscopic biopsy devoid of mucosa is usually considered inadequate for assessment [1].

Attached to this concept, using special pinch forceps, with or without a central spike, biopsies may be taken using either single (SBB) or double bite (DBB) techniques [5].

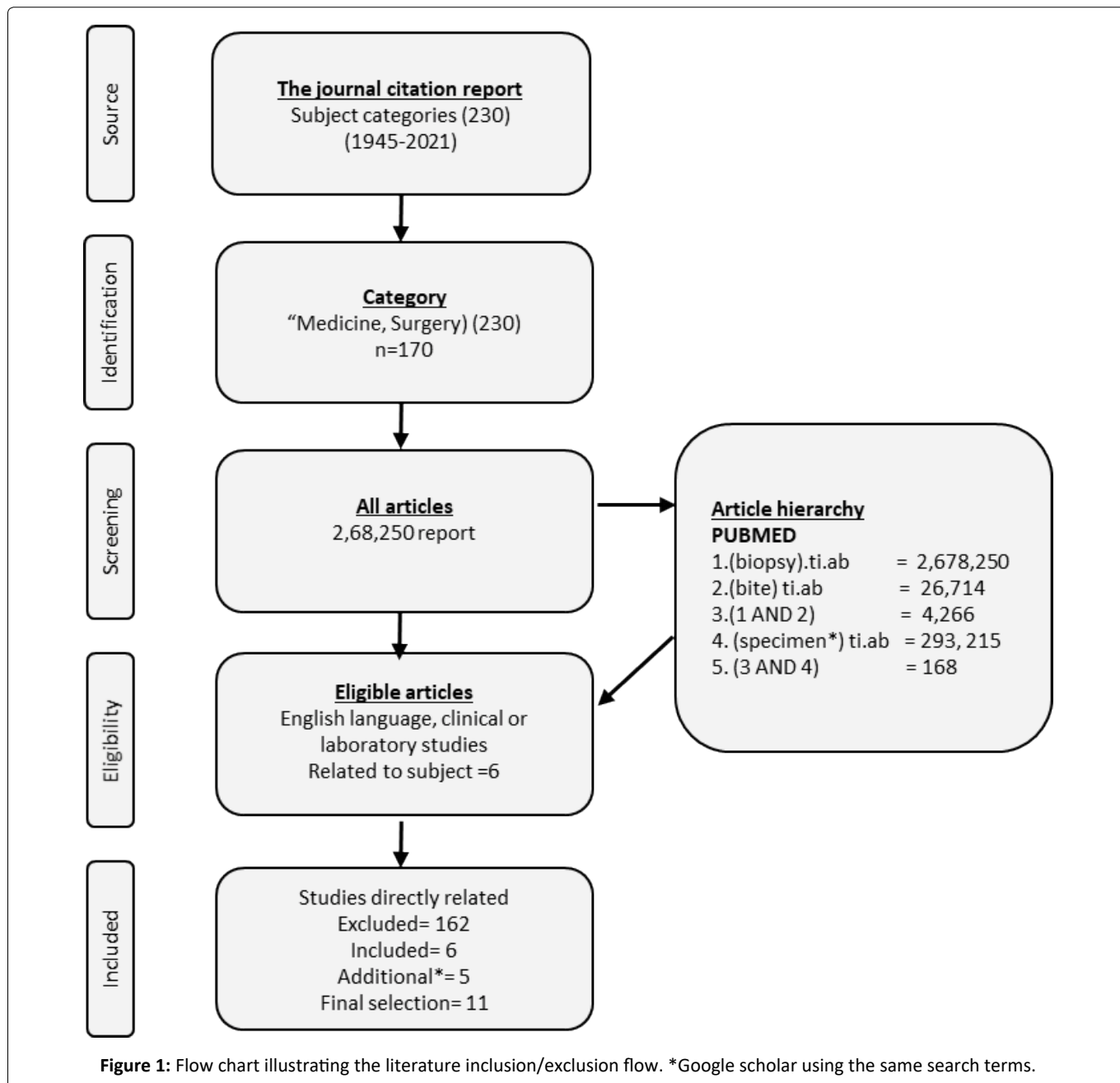
Considerable controversy exists in the manner of collection of biopsies. This is because of a perception that taking DBB biopsies may cause distortion or misalignment, hence, leading to diagnostic error. Equally, taking DBB may well reduce intubation time, and so complications associated with the procedure itself. Identifying the evidence behind both SBB and DBB may help endoscopist to weigh the pros and cons of histopathological accuracy and endoscopic time and this may change practice in a way that best serves the interest of

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patients. Therefore, the aim of this review is to consider the way biopsies are taken during gastrointestinal endoscopy.

## Results

A total of 168 articles were identified from PubMed and after a detailed assessment, six papers met the search criteria. A further five were identified from google scholar and the final number of articles included in the study was 11. Figure 1 and Table 1 summarise the search strategy and results in a flow diagram.

## Discussion

The studies cited above (Table 1) have all considered the issue of biopsy techniques i.e. SBB and DBB or multi-bite from different anatomic regions i.e. stomach, small or large intestine, in both human and animal models spanning different geographic regions across the world. Since the

approach in studies is different the features will be highlighted in a thematic rather than chronological manner.

## Comparison of protein quantity of biopsy specimen

Using a colorimetric technique, Frimberger, et al., [7] compared the protein content, a surrogate marker for adequacy of tissue, of biopsies collected through SBB (n = 79) and DBB (n = 79) techniques. Specimens were obtained from multiple regions i.e. Duodenum (n = 3), antrum (n = 10), corpus (n = 18), rectum (n = 30), sigmoid colon (n = 9) and colon (n = 9). They reported increased mean protein content (43%, p < 0.01) with DBB (66% specimens). Although, the study is a balanced randomised design with representative samples from all regions, it used an indirect assessment of tissue quantity and may lack histopathological and clinical applicability, the main issues in question.

**Table 1:** Studies examining comparison of biopsy techniques in both human and animal models.

Study and Methods	N	Results	Comments
Frimberger, et al. [6] Compares the sample size of a SBB (n = 79) with the sample size of a DBB (n = 79) colorimetric measurement of protein quantity was done. Spiked and un-spiked forceps used.	158	DBB increased the average protein content by 43% (p < 0.01). Forceps with a spike yielded a double sample in every case.	Balanced randomised design with representative samples from all regions yet it is an indirect study. Clinical is questionable.
Padda, et al. [8] Prospectively assess the adequacy of mucosal biopsy specimens (n = 288) i.e. SBB and DBB.	16	No difference between DBB (n = 192) and SBB (p < 0.05). SBB more prone to loss.	One pathologist, hence, no intra-observer variability. It was, however, a low powered the power study.
Fantin, et al. [9] Prospective, partially blinded, and randomized. Multi-bite (n = 510) and conventional (n = 520) forceps. Diameter, depth, artifacts, orientation, diagnostic quality.	250	Specimens obtained with both forceps are comparable in relation to diagnostics quality (p < 0.05).	Better definition of histological standards i.e. diameter, depth, artefacts, orientation. The study evaluated the efficacy multi byte forceps rather than technique per se.
Chu, et al. [10] It was well designed prospective study (n = 240) and the pathologists were blinded. Compared for SBB DBB.	40	No difference noted. Larger specimens were collected with alligator forceps and SBB saves time.	Detailed definition of histological standards was given. Evaluated the efficacy forceps rather than technique.
Zaidman, et al. [11] Porcine models comparing SBB and multiple bites for time taken and tissue quality. Pathologists (x2) blinded.	36	Multi-bite forceps faster (8.5 M) in comparison to SBB (13.3 M). No histological differences noted.	Indirect study where animal model was used. DBB was not compared.
Edery, et al. [13] Canine model comparing depth, crush artifacts and diagnostic using SBB and multi-bite forceps.	21	Gastric (n = 21) and duodenal (n = 20) biopsies and no significant difference was noted.	Indirect study where animal model was used. DBB was not compared.
Stern, et al. [12] Comparing diameter, depth, crush artifacts and specimen loss in SBB and DBB upper, lower GI tract.	29	OGD (n = 18) and Colon (n = 11). SBB (n = 69) larger than DBB (n = 59) (p < 0.05). No difference noted.	The study collected specimens from different regions. Low powered study and lack of full publication.
Hookey, et al. [14] To determine the effectivity of DBB in detecting dysplasia in ulcerative colitis. Two pathologists blinded to the biopsy technique examined each biopsy.	12	DBB specimens were inadequate for dysplasia assessment (OR = 2.78, 95% CI 1.37 to 5.59; P < 0.05). Tissue loss was more in DBB.	Clinically relevant study. The power of the study was low, and dysplasia is a patchy pathology in UC, hence comparison might have been biased.
Pappas, et al. [18] Yield of SBB and DBB for Surveillance of HDGC and comparison of time taken to collect biopsies. Prospectively randomized.	25	DBB size < SBB (2.5 mm vs. 3.0 mm; P < 0.001) but did not affect the surveillance. Time taken by DBB < SBB (p < 0.05).	Only used biopsies in one region which may have affected measurements of biopsy time i.e. taking biopsies in stomach is relatively easy.
Latorre, et al. [16] To compare DBB and SBB for orientation, consecutive crypt-to-villous units, and Marsh score DBB in patients with confirmed (n = 40 and suspected coeliac disease (n = 31).	86	66% of patients with the single-biopsy technique and 42% of patients with the double-biopsy technique had good orientation (P < 0.01).	Decisive conclusion to use only SBB method but the study excluded duodenal bulb biopsies from analysis which is used in the diagnosis of coeliac disease.
Amaro, et al. [7] USA To compare DBB and SBB in terms of the histologic evaluation of the small bowel biopsy.	30	SBB (70%) > deep DBB (65%) but no difference between the histologic diagnosis of small bowel.	SBB were better quality wise. The study only examined one area i.e. small bowel.

**Abbreviations:** M: minutes; GI: Gastrointestinal; OGD: Oesophago-Gastro-Duodenoscopy; HDGC: Hereditary Diffuse Gastric Cancer

## Studies comparing the histological qualities of biopsy specimens

Several studies have compared the histological quality of tissue specimens. Amaro, et al. [7] compared small bowel biopsies and reported overall superiority of SBB specimens but the biopsies were collected from the small intestine only. Similarly, Padda, et al., [8] in their prospective randomised study (n = 16) directly compared the histological quality of SBB (n = 96) and DBB (n = 196) biopsy and no histological

differences were reported. The study was a well designed prospective analysis and used one pathologist, thus reducing intra-observer variability in reporting. It was, however, low powered and only collected species from two regions. Later, Fan tin and Colleagues [9] improved on the design by defining the term histological quality which included; diameter, depth, artefacts, orientation and diagnostic quality of specimen. They too did not report any difference between, SBB (n = 510) and DBB (n = 520).

Chu, et al., [10] in contrast to the above two studies, compared histological quality in terms of; size, crush artefact, depth, adequacy, weight and overall rating in biopsies collected with forceps with needles. It was a well-designed prospective study (n = 240) and the pathologists were blinded, but the study only compared only gastric biopsies. Anecdotally, gastric biopsies are easy to take. Following this, Zaidman, et al., [11] studied multi-bite pelican forceps in collection of porcine specimens in a study (n = 2, biopsy = 36), comparing SBB, DBB and multi bite forceps and did not report major differences in histological quality. However the pathologists were not blind to the techniques of biopsy collection. This finding was confirmed in a conference paper (n = 142) [12] and by a study (n = 21) using canine specimens [13]. However the purpose of the quoted studies [9-11,13] was the comparison of different types of forceps *per se*, and not the technique i.e. SBB and DBB.

### Studies comparing the histological quality in context of a defined GI pathology

Hookey, et al., [14] conducted a prospective equal arm randomised and blind study comparing the evaluation of histological specimens for dysplasia in ulcerative colitis (n = 12), in specimens (n = 468) collected through SBB and DBB. They noticed DBB specimens were comparatively inadequate for assessment of dysplasia when compared to tier counterpart, SBB (OR = 2.78, 95% CI 1.37 to 5.59; P = 0.005). The study design, conduct and methodology are different in that an important clinical outcome i.e. dysplasia detection was under question. Dysplasia is patchy in UC [15]. Which may mean that a specimen collection bias could have affected the study.

Latorre, et al., [16] in a prospective cohort and blinded study examined the histological orientation of the biopsy specimen obtained through either SBB or DBB from the duodenum of patients (n = 86) with suspected (n = 47%), known (n = 36%) Coeliac disease (CD) and (n = 17%) controls. SBB yielded well oriented specimens in 66% patients and DBB returned in 42% (p < 0.01) and matched pairs showed improved orientation with the SBB (OR 3.1; 95% CI, 1.5-7.1; P < 0.01). The study was well designed and blinded; however, similar to Hookey, et al., [14] it only examined one specific region. Furthermore, duodenal cap biopsy specimens which are useful in the diagnosis of CD were excluded [17].

Finally, Pappas, et al., [18] did not report any histological difference between biopsy technique (n = 48) in a surveillance study for hereditary diffuse gastric cancer.

### Studies comparing the time taken to take biopsies

Several studies compared the time taken to collect biopsies. Zaidman, et al., [11] reported that SBB took relatively longer but it is noteworthy that this study was based on a canine model. A recent study, using gastric biopsies, compared time taken between the two techniques and reported reduced overall time for biopsies taken through DBB [18]. It may be noted that it is easy to take gastric biopsies hence time taken per

biopsy cycle may well be constant and predictable, whereas, time taken for colonic and oesophageal biopsies may not be predictable per cycle. This is because of the technical difficulty in colonic biopsies if specimens are taken from a difficult fold or the endoscope reaches the target area on an unstable loop. Oesophageal biopsies are prone to loss or difficult to take.

### Studies comparing the specimen loss

Specimen loss was an aim in several studies. Although, Frimberger and colleagues [6] reported relatively less specimen loss with spiked forceps it was not the comparison of technique *per se*. Padda, et al., [8] reported relatively increased first specimen loss (25%, p = 0.02) with DBB and the loss was worse with non-spiked forceps (28.1% vs. 13.3%; p = 0.01). It is interesting to note that oesophageal samples were relatively more prone to loss as compared to gastric specimens. Although Stren, et al., [12] has referred to significant sample loss with DBB technique, figures given are not objective. Hookey and colleagues [14] reported that 14 biopsy specimens (6.0%) were lost in DBB as compared to eight (3.4%) SBB specimens (OR 1.8, 95% CI 0.69 to 5.04; P = 0.27). An objective comparison of lost specimens needs to be undertaken using different regions in a randomised study.

### Material and Methods

This seems an odd place to put this after the results.

### Literature and search strategy

A scoping literature search was conducted in September 2021 using PUBMED. The following terms were applied, searching for titles and abstract (TiAb): (biopsy).TiAb, AND bite AND specimen. Moreover, using the same search terms in Google scholar further unique articles (n = 5) were identified. Additionally, one conference presentation was also included.

### Ethical approval

No ethical approval was required for this scoping review.

### Conclusion

There is significant methodological inconsistency and variations in the studies cited above. Frimberger, et al., [6] used multiple regions but their study lacked clinical application as they measured protein content only. Other studies have been based on animal models [10,11]. Some authors have compared techniques indirectly [9,13].

The exact clinical value of either taking DBB or SBB is not clear from the studies cited above. This is because, using a large prospective sample, none has specifically assessed the diagnostic or prognostic value of these techniques but one may infer that taking biopsies by either method does not matter much.

There is a lack of a clinical study which, simultaneously, taking multi-regional samples, examines histological adequacy, time taken to complete the biopsy cycles and specimen loss in a holistic manner. This will, as anticipated, give clear guidance to the endoscopists to adapt a standardised method of taking endoscopic samples.

## Authors' Contribution

Conceptualization: HM, SO, JFM; Methodology: HM, SR, SA, JFM; Formal analysis: HM, SA, SO JFM; Writing original draft preparation: HM, SO; writing review and editing: HM, SO, SA, JFM.

All authors have read and agreed to the published version of the manuscript.

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## Conflicts of Interest

The authors declare no conflict of interest.

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