

# Fine-needle aspiration (FNA) biopsy: historical aspects

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**Abstract:** This study aims to present the origins and the historical evolution of fine-needle aspiration biopsy and to also underline its importance in the history of modern cytology. The article focuses on the advances made in the 20<sup>th</sup> century that have led to the modern techniques associated with the procedure. The authors conducted a thorough review of early reports on needle biopsy, particularly those published during 19<sup>th</sup> and 20<sup>th</sup> century, examining in brief also the origins of the needle biopsy. The first report on the use of needle puncture is referred in early writings of Arab medicine. In the early 20<sup>th</sup> century, Martin and Ellis are considered to be the founders of modern needle aspiration techniques. The German doctor Mannheim was the first to publish reports suggesting the use of fine needles with a small gauge. The establishment and world-wide expansion of FNA should be attributed to the representatives of the Swedish School of Cytopathology. The school embraced FNA in the second half of the 20<sup>th</sup> century while serving as a training ground for doctors around the world. The history of needle biopsy spans ten centuries. However, the development and establishment of the technique in its modern form took place primarily during the twentieth century. Today, FNA is considered an important cytologic technique with sufficient diagnostic accuracy, especially when applied in cases of lung and prostate cancer.

**Keywords:** aspiration biopsy, history, cytopathology, diagnostic cytology, needle aspiration

## Introduction

Fine-needle aspiration (FNA) biopsy is the study of cells obtained by puncturing organs of human body with the use of small-gauge needle [1]. Doctors usually perform the procedure after detection of a mass lesion through imaging methods such as ultrasound tomography, CT or MRI [2]. The process of aspiration biopsy involves the puncture of the lesion with the use of a fine needle (22-gauge needle) of various lengths (from 5 cm to 20 cm) with external diameters between 0.6 mm and 1.0 mm [2]. Aspiration biopsy cytology currently constitutes a separate branch of diagnostic cytology [3,4]. The main philosophy of aspiration biopsy cytology differs greatly from exfoliative cytology, since that procedure focuses on cells that have been scraped or peeled from epithelium or mesothelium. The history of the technique needle biopsy spans a period of over 10 centuries (Table 1), whereas FNA undergone a great deal of improvements during the last century. This article will document the development of FNA techniques during the 20<sup>th</sup> century.

## The first use of needle for the diagnosis and treatment of various diseases.

The first report on the use of needles for therapeutic purposes can be found in Arab medicine, in the writings of Albucasis or Abu al-Qasim Khalaf ibn al-Abbas Al-Zahrawi as it was his Arab name (936-1013 A.D), court physician to the caliph of the Andalusia, Al-Hakim II. In his famous treatise, Kitab al-Tasrif (The Method of Medicine), the most influential book of Arab Medieval Medicine, Albucasis described for the first time therapeutic punctures of the thyroid gland, using instruments resembling modern aspiration needles [5-7]. Albucasis' description resembles a modern FNA of the thyroid gland [8]:

"This tumor, which is called 'Elephant of the throat,' is a large tumor the color of the body; it commonly occurs in women. It is of two kinds, congenital and acquired. There is no treatment for the congenital type. The acquired type consists of two kinds: one resembles a sebaceous cyst while the other resembles a tumor arising from an arterial aneurysm. The latter is dangerous to incise, so never you apply a knife to the latter kind unless the tumor is very small. If you try to explore them with a probe and find they are like sebaceous cysts and not attached to any blood vessel, then

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immediately cut down upon them as you would a cyst and remove them with whatever capsule may surround them, as long as they are contained within a capsule. If not, dissect away the whole accurately; then treat the place with suitable remedies."

Kitab Al-Tasrif was considered a medical encyclopaedia concerning surgery. The 10<sup>th</sup>-century text contains figures of numerous surgical instruments and even medical needles. Some of the needles are clearly hollow, representing the first documented needles in the history of Medicine. The work by Albucahis was so influential that his book was translated into Latin by Gerard of Cremona (1114-1187 A.D.), a famous translator of Arab scientific works. The French surgeon and "Restorer of Surgery," Guy de Chauliac (1300-1368 A.D.), in his famous book "Inventarium Sive Chirurgia Magna" quoted the work of Albucahis more than 200 times [9].

### Needle biopsy in the twentieth century: The founders of the fine needle aspiration (FNA) technique

During the 19<sup>th</sup> century, and the beginning of the 20<sup>th</sup> century, the use of surgical needles for the diagnosis and treatment of various diseases was widely used [10-16].

In 1912, a German haematologist, Hans Hirschfeld (1873-1944), reported the first needle aspiration biopsy by reporting the diagnosis of cutaneous lymphomas and other tumors with the use of needle aspiration biopsy and histological process of the acquired cellular material [17]. In his paper entitled 'Über isolierte aleukämische Lymphadenose der Haut', he described his technique in a very detailed way (translated in English): "One of the largest facial tumors is punctured. It is not possible to aspirate any fluid and so the blood drops emerging from the puncture are taken for dry preparation on a slide. Staining with May-Giemsa produced their picture..." [17]. Hirschfeld described the use of small tissue samples that were excised from the tumors and then fixed in formol and stained with various staining methods.

Gordon Ward, a British haematologist and medical officer in the British Army, improved and expanded the method in 1914 to diagnose lymphoblastoma [18]. Hirschfeld also extended his investigations to other tumors and published his observations in 1919 [19].

In 1916, Anastasios Aravandinos, professor of Internal Medicine in Athens University, designed a needle for the safe procedure of spleen puncture and the quick aspiration of cellular material [20]. Similar punctures were performed during his time for the diagnosis of non-neoplastic liver lesions (*i.a.* cysts) as well as for the diagnosis and therapy of liver abscesses for tropical diseases, such as histolytic amoeba infection.

While working at John Hopkins Hospital in Baltimore, Guthrie, performed a systematic study of cellular smears from lymph node puncture in 1921 [21]. He used a 21-gauge needle for aspiration biopsy and coated aspirates on glass slides forming cell films that were air dried and stained with Romanowksy staining. Guthrie reported that the method allowed him to successfully diagnose various diseases such as syphilis, tuberculosis, malignant lymphoma, leukemia and metastatic carcinoma [21].

Leonard Stanley Dudgeon (1876-1938), a pathologist working at St Thomas' Hospital in London and Professor of Pathology in University of London, was the first to scientifically establish the technique of needle biopsy [22,23]. Dudgeon's motive was the need to establish a fast and secure diagnosis of histological preparations. He mounted tissue material from surgical biopsies to glass slides by using touching smears or imprints. In his paper with Vincent Patrick [22], a resident assistant surgeon in St. Thomas Hospital, they reported 300 cases with a diagnostic accuracy of 97 percent. They describe a total of 9 erroneous diagnoses of which six occurred from the first 100 samples, and three in the second 100 samples; the erroneous cases included two cases of ulcers of the lower lip (a septic ulcer and an actual carcinoma), one case of a node isolated from peritoneum, two cases of lymphatic glands which were examined for metastatic carcinoma and four cases of breast tumors. His later study with Norman Barrett (1903-1979), an Australian-born British surgeon at St. Thomas Hospital, in 1934 [23] focused mainly on the cytology of scrapings from 1.000 surgical specimens. In this study, Dudgeon concentrated on the possibility of identifying malignant cells in sputum using smears fixed with Schaudinn's solution and stained with haemalum and eosin. Over time, he perfected this technique. In a later paper with C.H. Wrigley, [24] he presented a positive detection rate of 68 percent in a lung cancer study, finding malignant cells in the sputum in 26 out of 38 cases.

Two researcher groups in the United States [25-27], Bradley Coley with Sharp and Hayes Martin with Edward Ellis (1877-1954), worked independently on the same method at the Memorial Hospital in New York City.

Independently from each other, the two groups began experimenting on a large scale with aspiration biopsy of various human tumors in the late 20s. In a personal letter to Koss, [28] Dr. Fred W. Stewart said that Dr. James Ewing (1866-1943), chief of pathology at Memorial Hospital, initially opposed incision biopsies of cancers because of his firm belief that the procedure considerably increased the risk of spread of the disease. In fact, during Ewing's tenure as a director of the Memorial Hospital, open biopsies of subcutaneous tumors, whether primary or metastatic, were

prohibited [29]. Stewart, the successor of Ewing, wrote that: "The needle evolved as a sort of compromise." [29]

Both Martin and Coley were reluctant to treat patients without a firm diagnosis, so aspiration biopsy evolved as a method to diagnose cancer without cutting invasive surgery. Martin and Ellis also wanted to combine cellular and histological findings and also simplify the method for studying biopsy specimens. In the early thirties, they applied their technique on breast, thyroid gland and stomach carcinomas, as well as myelocytomas and non-neoplastic diseases [26,27]. After infiltration with 1 percent novocaine, the procedure consisted of a small incision over the lesion with the use of a scalpel (No. 11 Bard Parker blade), followed by aspiration with an 18-gauge needle attached to a 20-ml Record syringe. The aspirated cellular material was smeared on glass slides, air-dried and stained with hematoxylin and eosin (immediate method). Fragments of tissue obtained by the procedure were removed, placed on a piece of blotting paper (a so-called "clot"), fixed in formalin and processed as a usual biopsy (longer method) [26-28]. The immediate method, yielded tissue samples in 80 percent of the cases, with a total of 65 cases identified with cancer; 60 percent of them were also confirmed by histological diagnosis. In the conclusions of their paper, Martin and Ellis [26] refer to the advantages and the disadvantages of their method: "Biopsy by aspiration has, we feel, few, if any, disadvantages to the patient from the surgical standpoint. The interpretation of the histological picture (especially of the smears) requires both an experienced and sympathetic pathologist. Undoubtedly, larger specimens uniformly fixed and stained offer more satisfactory material upon which to render a definite opinion, but such a preparation can too often be obtained only at considerable disadvantage to the patient or too late to be of any particular value in outlining treatment ... We do not advocate this method of biopsy in any case where larger specimens of tissue can be readily and safely secured by any other method".

In 1930, Ferguson [30] started to apply the technique developed by Martin and Ellis in the study of prostate lesions from cytological specimens obtained with a perineal puncture technique. He noted that a positive diagnosis of prostate cancer by needle biopsy was reliable for an experienced pathologist.

A year later, Ernst Mannheim, a German pathologist, published a report entitled "Die Bedeutung der Tumorpunktion für die Tumordiagnose" ("The significance of tumor punctures for tumor diagnosis"). Mannheim's article should be considered the first report on the technique of fine needle aspiration biopsy (*i.a.*, featuring a needle with diameter of 1 mm). [31] Mannheim, who was aware of the work of Martin and

Ellis, wanted to avoid disease dispersion and to cause less harm to his patients. He characteristically noted in his paper (translated in English): "Another extensive report on our subject was published by Martin and Ellis. I noticed it only when I had already started my own investigations. However, these authors use a strong trocar, making an incision into the skin above the tumor prior to the puncture. Through aspiration they obtain so much tumor substance that they were able to embed and section small particles of tumor tissues. But this kind of punching is a rather heroic intervention affecting a considerable trauma; the risk of promoting growth and metastazation of tumors is by no means negligible" [31]. Worried about damage caused by the procedure, he considered examining less cellular material and proposed the use of a fine needle. Mannheim reported his findings in 43 cases, mostly breast cancer and neoplasms of the upper gastrointestinal system. He led the European school of fine needle aspiration biopsy, which completely modified the approach to this method of diagnosis. According to Koss, [28] Mannheim should be considered beyond any doubt as the "spiritual leader of the European school of thin needle aspiration biopsy, which was completely modified the approach to this method of diagnosis".

In 1933, Fred Waldford Stewart (1894-1991), who would later succeed Dr. Ewing in 1939 as Head of the Department of Pathology, reported the results of needle aspiration biopsy from 2,500 neoplasms [32]. His hallmark paper on aspiration biopsies interpreted the results of Martin, Ellis and Coley. Years later, according to Koss and Lieberman, he wrote that he "got damned by several people for writing it, without any proof" [29]. Stewart's study supplied the theoretical basis of fine needle aspiration biopsy by referring to clinical and laboratory associations and suggesting a comparative study of the material using the new technique as well as conventional histological preparations. He also referred to the limitations and potential errors of his technique and made mention not only of the cytomorphological characteristics, but also of the characteristics of the "architecture" of the aspired material. Although he favoured aspiration biopsies, he did mention the difficulties in fibrous alterations causing scanty aspirates and smears nearly void of any cells. He also discussed the problems involved in the diagnosis of sarcomas or various diseases of the thyroid gland and of the breast [32, 33].

In 1934, Martin and Ellis reported their experience with 1,405 diagnoses of cancer in 662 lymph nodes, 280 breasts, 140 bones, 41 lung tumors and 182 miscellaneous lesions [27].

Martin and Ellis also considered the use of Stewart's technique in clinical practice, especially for the study of inoperable neoplastic tissues located in inaccessible parts of human body [33,34]. According to

**Table 1.** Chronology of the events in the history of the use of needle in diagnosis and treatment

Year	Event	References
Circa 1000	Ab al-Kasim describes therapeutic puncture of thyroid gland	[5,7,9]
1833	Baron Dupuytren reports the diagnosis of echinococcus cyst by puncture aspiration	[36]
1833	Stanley also publishes the diagnosis of echinococcus cyst by puncture aspiration	[37]
1846	Kün publishes his paper, "A new instrument for the diagnosis of tumors," reporting the use of needle biopsy for cancer	[10]
1851	Lebert reports the use of needle biopsy for cancer	[11]
1851	Skey performs needle biopsies in breast cysts	[38]
1853	Sir James Paget and Erichsen use needle biopsy for the diagnosis of breast tumors	[39]
1853	Pravaz and Gabriel design a needle for aneurysm's puncture	[13]
1863	Pritchard performs needle biopsies using a grooved needle to puncture breast lesions	[38]
1865	Zagarolas performs liver punctures on liver abscesses	[40]
1883	Leyden uses puncture biopsy techniques to diagnose pneumonia of microbial etiology	[12]
1886	Ménétrier diagnose malignant tumors by needle biopsy	[14]
1887	Kröning diagnose malignant tumors by needle biopsy	[15]
1904	Greig and Gray perform aspiration biopsy to diagnose trypanosomiasis	[16]
1907	Proscher performs aspiration biopsy to diagnose syphilis by identifying spirochaetes in lymph nodes	[38]
1909	Horder performs aspiration biopsies for lung diseases	[41]
1912	Hirschfeld publishes his paper on biopsies from lymph nodes	[17]
1914	Ward diagnoses lymphoblastoma by aspiration biopsy	[18]
1914	Chatard and Guthrie diagnose trypanosomiasis by lymph node aspiration biopsy	[42]
1916	Aravadinis designs a special needle for safe spleen puncture	[20]
1918	Deelman publishes a paper about the puncturing of tumors	[43]
1919	Hirschfeld expands his histological studies on needle biopsies	[19]
1921	Guthrie diagnoses syphilis, tuberculosis, malignant lymphoma, leukemia and metastatic carcinoma by lymph-node puncture	[21]
1927	Müller publishes a paper on the diagnosis of cancer and tuberculosis by puncturing	[44]
1927	Forckner publishes a paper on puncturing of lymph nodes	[45]
1927	Dudgeon and Patrick publish their first paper describing the use of fine-needle biopsy techniques for the diagnosis of tumors	[22]
1927	Arinkin publishes a paper on the investigation through puncturing of bone marrow	[46]
1930	Martin and Ellis publish their first monumental paper on aspiration needle biopsy	[27]
1930	Ferguson applies needle puncture on the diagnosis of prostatic neoplasms.	[30]
1931	Coley and Sharp use needle aspiration for the diagnosis of bone tumors	[25]
1931	Mannheim is the first to suggest the use of fine needle for aspiration biopsies	[31]
1933	Stewart publishes his paper on the diagnosis of tumors by aspiration	[32]
1934	Martin and Ellis publish their second hallmark paper on aspiration biopsy.	[27]
1935	Frola applies puncturing to diagnose liver diseases	[47]
1936	Martin and Stewart publish a paper on the advantages and limitations of aspiration biopsy	[34]
1936	Rohr and Hegglin apply needle puncturing in order to diagnose cancer metastases in bone marrow	[48]
1937	Émile-Weil publish a paper on diagnosis of liver diseases with puncture	[49]
1942	Francke publishes his observations on the diagnosis of tumors from aspirated material	[50]
1942	Sayago publishes a paper on aspiration and surgical biopsies	[51]
1946	Pascyro publishes a paper on the applications of cytology and puncturing in haematology	[52]

Table 1. (continued)

1948	Tempka reports his observations on lymph node aspiration biopsies	[53]
1948	Piaggio-Blanco publishes a paper on thyroid gland aspiration biopsies	[54]
1949	Budd reports on the application of FNA in breast lesions	[55]
1949	Saphir applies FNA in the diagnosis of cancer from pleural and peritoneal fluid	[56]
1950	Piaggio-Blanco and Paseyro publish their observations on the application of FNA on breast lesions	[57]
1952	Söderström publishes his paper on puncture of goiters.	[58]
1954	Lopes Cardozo publishes his "Clinical Cytology"	[59]
1955	Comillot and Verhaeghe publish a paper on the diagnosis of central tumors	[60]
1955	Ludin reports on the use of organ puncture in clinical diagnostics	[61]
1958	Söderström publishes a paper on the identification of normal tissues and tumors by cytologic aspiration biopsy	[62]
1960	Franzen applies the technique of transrectal biopsy for prostate cancer	[63]
1961	Koss publishes his "Diagnostic Cytology and Its Histopathological bases"	[64]
1966	Dahlgren and Nordenström publish a monograph on transthoracic needle biopsy	[65]
1966	Söderström publishes a monograph on FNA biopsy	[66]
1970	Paseyro publishes his monograph of Clinical Cytology	[67]
1974	Esposti publishes his monograph entitled "Aspiration biopsy cytology in the diagnosis and management of prostatic carcinoma"	[68]
1975	Lopes Cardozo publishes his second monograph "Atlas of Clinical Cytology"	[69]
1974/1979	Zajicek publishes his monograph Aspiration Biopsy Cytology	[70, 71]
1981	Lowhagen and Willems publish a monograph on the application of FNA in thyroid diseases	[72]
1981	Kaminsky publishes his monograph on aspiration biopsy	[73]
1981	Zornosa publishes a monograph entitled "Percutaneous Needle Biopsy"	[74]
1981	Wittenberg and Ferucci publish a monograph on the interventional radiology of the abdomen	[75]
1983	Frale publishes a comprehensive review on FNA.	[2]
1988	Kline publishes a monograph entitled "Handbook of Fine Needle Aspiration Cytology"	[1]
1989	Linsk and Franzen publish their classic "Clinical aspiration cytology"	[76]

Martin and Ellis, one of the advantages of needle biopsy over conventional surgical approaches for the histological diagnosis of tumors is the avoidance of cancerous cell dispersion. Other studies further supported this advantage [34].

Martin and Stewart collaborated on a 1936 report on the indications, advantages and limitations of needle biopsy [34]. Reading their paper, one can understand that Martin's influence was stronger, leading to the overall conclusion in favor of aspiration biopsy which downplayed Stewart's earlier reservations.

Grunze and Spriggs conduct a short comparison between the work of Dudgeon's and Martin's teams [35]. Dudgeon's team never worked on material from aspiration biopsy and never performed any punctures for diagnostic purposes. On the contrary, they were primarily focused on the development of cytological techniques, such as the imprint and wet film technique, which were also used later in combination with fine needle aspiration biopsy [22,23]. Dudgeon's wet film

technique secured a better preservation of cellular material, but Martin, Ellis and Stewart developed the true technique of needle biopsy. The latter team's work was mostly associated with histological diagnosis since they were more interested in the acquisition of tissue than cellular material [26]. Both Dudgeon and Patrick [22] and Martin and Ellis [26] used histological staining protocols (varieties of hematoxylin-eosin staining) that were not appropriate for the study of the cytoplasm. Dudgeon and Patrick used haemalum and eosin as counterstain, whereas Martin and Ellis used haematoxylin and eosin.

## Epilogue

In conclusion, the first report on needle biopsy dates back to the 11<sup>th</sup> century, in the texts of the Arab doctor Abulcasis. However, the 20<sup>th</sup> century should be considered the most crucial period in the history of FNA. Dudgeon was the first to establish aspiration biopsy on

a scientific basis, while Martin and Ellis applied needle biopsies on a wide range of samples and clinical cases. But, the first report on the use of fine, 22-gauge needle should be attributed to Manheim. The elaboration of FNA by the Swedish school in the forthcoming years was crucial for the establishment of the technique and its world-wide acceptance.

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