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Filippo Pacini: A Determined Observer

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ABSTRACT: The life of Filippo Pacini (1812–1883) and his major scientific achievements are outlined. Pacini drew attention to the corpuscles named after him in 1831, when he was a medical student, and had to struggle for many years to convince the scientific community of the reliability and importance of his findings. In 1849 Pacini became professor of anatomy at the University of Florence. Creative scientist, innovative teacher, well aware that the use of the microscope represented a revolutionary approach, Pacini pursued histological studies until his death. He also first discovered in 1854 (30 years before Robert Koch) the causative agent of cholera, and firmly believed that the disease was contagious. Strong-willed, modest, and poor, Pacini received from his colleagues more recognition in the obituaries than during his life.

KEY WORDS: Pacinian corpuscles, History of neuroscience, Infectious diseases.

INTRODUCTION

Pacinian corpuscles are primary mechanoreceptors that play a role in the sensation of touch. These relatively large receptors (whose long axis is about 2500 μm in humans [1]) can even be seen with the naked eye, and their description dates back at least to the 18th century. Filippo Pacini, unaware of previous reports, rediscovered the corpuscles that were named after him, and struggled to bring his findings to the attention of the scientific community. Pacinian corpuscles were the first specialized end organs in the skin to be identified, although their functional role in sensation was identified only much later [8].

This article is aimed at providing a brief overview of Pacini's contribution to science and to neuroscience in particular.

THE FIRST DESCRIPTIONS OF PACINIAN CORPUSCLES

Johannes Gottlieb Lehmann [13, cited in ref. 1] is credited for the description of Pacinian corpuscles in his Doctoral thesis in 1741. It is, however, commonly recognized [4,8] that Pacinian corpuscles were first observed in the same year by the German professor of Anatomy and Botany, D. Abraham Vater (1684–1751). Without providing any structural description, Vater made a drawing of the lamellar corpuscles (the original specimens were preserved in the Anatomical Museum of Göttingen) and classified them as *Papillae Nerveae*, attached in large quantities to the

digital nerves [21]. These observations seem to have been then forgotten for many decades.

The lamellar corpuscles were again identified by John Shekleton (1795–1824). As reported recently [20], the corpuscles were dissected out, together with many other pieces of dissection, while Shekleton was the curator of the Museum of the Royal College of Surgeons in Ireland between 1820 and 1824. Shekleton's findings were published by Smith in 1848 [19], when Pacini's reports had already appeared.

PACINI'S BIOGRAPHICAL SKETCH

The following data on Pacini's life and studies on the lamellar corpuscles are derived from Coturri [5,6] and one of Pacini's students, Aurelio Bianchi, who collected for the National Library of Florence Pacini's manuscripts after his death [2]. Filippo Pacini (Fig. 1) was born in Pistoia, in Tuscany, on May 25, 1812. He was of humble origin (his father was a cobbler) and received a strict religious education. His family wanted him to become a bishop and committed him to religious studies. Pacini, however, soon abandoned the ecclesiastical career. In 1830 he was awarded a scholarship and admitted to the famous "Scuola Medica Pistoiese," founded in 1666 by the Ospedale del Ceppo in Pistoia. At this medical school Pacini attended the basic courses with excellent results, becoming a very experienced dissector.

In 1849 Pacini obtained the chair of General and Topographic Anatomy at the University of Florence, which he held until his death. Pacini never married, and for a long time took care of his two sisters, both seriously ill. He spent all his money in assisting his sisters and supporting his own studies. Pacini died, very poor, on July 9, 1883.

THE REDISCOVERY OF PACINIAN CORPUSCLES

In 1831, attending as an "intern student" the dissections in the anatomy course of the second year of medical school, Pacini observed some small ovoidal bodies attached to the digital branches of the median and ulnar nerves, hardly visible to the naked eye. "What are these?" he asked to his professors, and was very unsatisfied by the answer: "Small globules of fat tissue." Pacini did not find any mention of the corpuscles in his anatomy textbooks. Very determined and hard-headed, he used all his savings to buy a small microscope with a wooden tube and acromatic lenses, providing a 30 times magnification, and began to investigate on his own the morphology of the small

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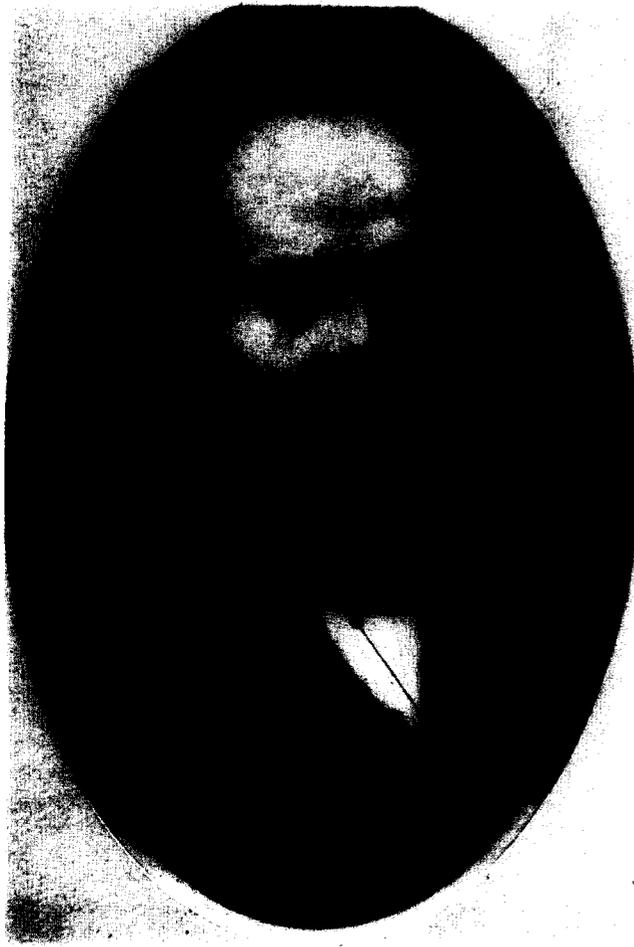


FIG. 1. Portrait of Filippo Pacini ca. 1870.

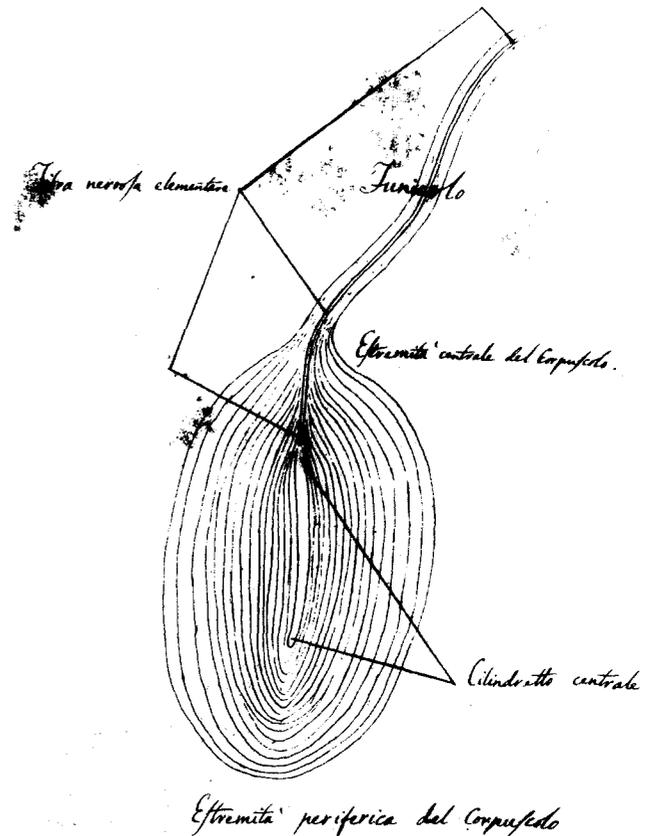
corpuscles. Convinced that the hand corpuscles were related to nerve fibers, Pacini defined them as "tactile ganglia." In 1833 he found the same corpuscles between the dorsal surface and the large vessels of the pancreas.

In October 1835 Pacini submitted a scientific communication to the Società Medico-Fisica Fiorentina (Medico-Physical Society of Florence). In this manuscript [15] he reported the identification of the small corpuscles connected with the digital nerves and also distributed in different splanchnic regions: "small ellipsoidal globose corpuscles, just like a cyst with an inner pulpy and white substance, moistened by a limpid fluid; their larger diameter is crossed by a little streak which is whiter than the remaining part of the corpuscle." The original report was read by the secretary of the Medico-Physical Society during the session held on November 22, 1835; the reaction of the audience was very cold, and Pacini's findings did not raise any interest. However, his research activity did not seem to suffer much from such indifference, and Pacini insisted in presenting further observations to a scientific congress held in Pisa in 1839. On that occasion, the congress President appointed an *ad hoc* committee to examine Pacini's data. The secretary of the committee (Francesco Puccinotti, professor of Internal Medicine at the University of Pisa) finally declared that the corpuscles did indeed exist, but it was unclear whether they were neural structures (as proposed by Pacini) or "tendinous-aponeurotic expansions."

In the meantime, also French scientists (Andral, Camus, and Lacroix) had observed the corpuscles in 1833 and provided a description in an anatomy textbook in 1836 [7]. Pacini was not aware of this report, and published *in extenso* his findings in 1840 [15], providing a drawing of the ovoid bodies formed by concentric lamellae, in which an "elementary nerve fiber" was coursing through a "funiculus" to the "central cylinder" of the corpuscle (Fig. 2).

In 1844 Pacini presented his work again at a congress in Lucca, describing the peculiar histological technique employed to visualize the corpuscles, which had been treated for 36 h with diluted nitric acid and ethanol. Pacini could thus demonstrate the "complete" structure of the corpuscles. He reported that the interlamellar spaces contained some fluid and that the lamellae were connected by a ligament (*Legamentum intercapsulare*) to the distal pole of the corpuscles. He also suggested that the corpuscles could represent "terminal ganglia related to the animal's bioelectrical activity."

In the same year (1844), the famous German histologist Jakob Henle (1809–1885) and his assistant, Rudolph Albrecht von Kölliker (1817–1905), published a detailed study on the corpuscles, which they named after Pacini [11]. Henle and Kölliker described that the lamellae consisted of cells and two different layers of



CORPUSCOLO DEL PACINI

Riproduzione a metà del vero del disegno autografo di Filippo Pacini
(*Mss. Pacini*, Vol. XX, c. 9).

FIG. 2. Pacini's first drawing of the lamellar corpuscles, made in 1840. Handwritten labels: Funiculus, elementary nerve fiber, central extremity of the corpuscles, central small cylinder, peripheral extremity of the corpuscle.

fibrillar tissue, the outer layer being transverse and the inner longitudinal. Henle and Kölliker also found blood vessels around and within the corpuscles and described the myelinated nerve fiber, which could divide into terminal branches, ending within them; they suggested that Pacinian corpuscles were "electric organs," comparable with those of some "electric" fish. Thus, Pacinian corpuscles had finally been christened, and their connection to a nerve fiber had been established.

In 1863 Pacini commissioned a set of anatomical models of the corpuscles from the Florentinian wax modeller Remigio Lei. Such models were prepared according to the artistic, and almost secret, traditions of the Wax Laboratory of the University Zoological Museum "La Specola," which possesses a remarkable and large collection of human and animal anatomy wax models. A plaster cast was added to the clay model. After its solidification, a large series of differently coloured wax layers were accurately settled down. Muscle fibers, blood and lymphatic vessels, as well as nerve fibers, completed the work. These unique wax models still display in all their striking perfection in the Anatomical Museum of the University of Florence (Fig. 3).

PACINIAN CORPUSCLES AFTER PACINI'S STUDIES

Mayer [14] performed preliminary physiological studies on the corpuscles. In 1876 Key and Retzius [11] presented in their monograph a large collection of drawings of the different types of Pacinian corpuscles throughout the human body. Detailed surveys of the older literature on Pacinian corpuscles and the first

hypotheses on their function can be found in refs. [1] and [4]. Bell et al. [1] also provided an updated review of the structure and function of Pacinian corpuscles. It has now been definitely established that these encapsulated nerve endings are widely distributed in the human body, where they are numerous in the skin and concentrated in the fingers, and have been found in many other structures (such as in articular capsules, on tendons and within muscles, near peripheral nerves, and in the urinary tract and bladder, as well as genital organs of both sexes). Pacinian corpuscles have also been described in many higher vertebrate species and are very numerous in the mesentery of the cat.

Light and electron microscopic studies (reviewed in ref. [1]) have elucidated that the Pacinian corpuscles are innervated by a myelinated axon, whose terminal segment is unmyelinated and has a bead-shaped ending. The neurite, that can divide in two or more endings, is surrounded by nonneuronal cytoplasmic layers arranged in concentric lamellae. The inner and outer cores, separated by an intermediate growth zone, form the inner capsule of the corpuscle. The lamellae of the inner core are very closely packed. The lamellae of the outer core are instead separated by relatively wide spaces, filled with fluid containing macrophages, collagen fibrils, and vascular capillaries. The inner capsule is enclosed by a few tightly packed lamellae and by connective tissue, which form the external capsule of the corpuscle. Each lamella consists of a single layer of tightly fitting cells of epithelial type.

It has now been established that cutaneous Pacinian corpuscles are quickly adapting mechanoreceptor responding to high

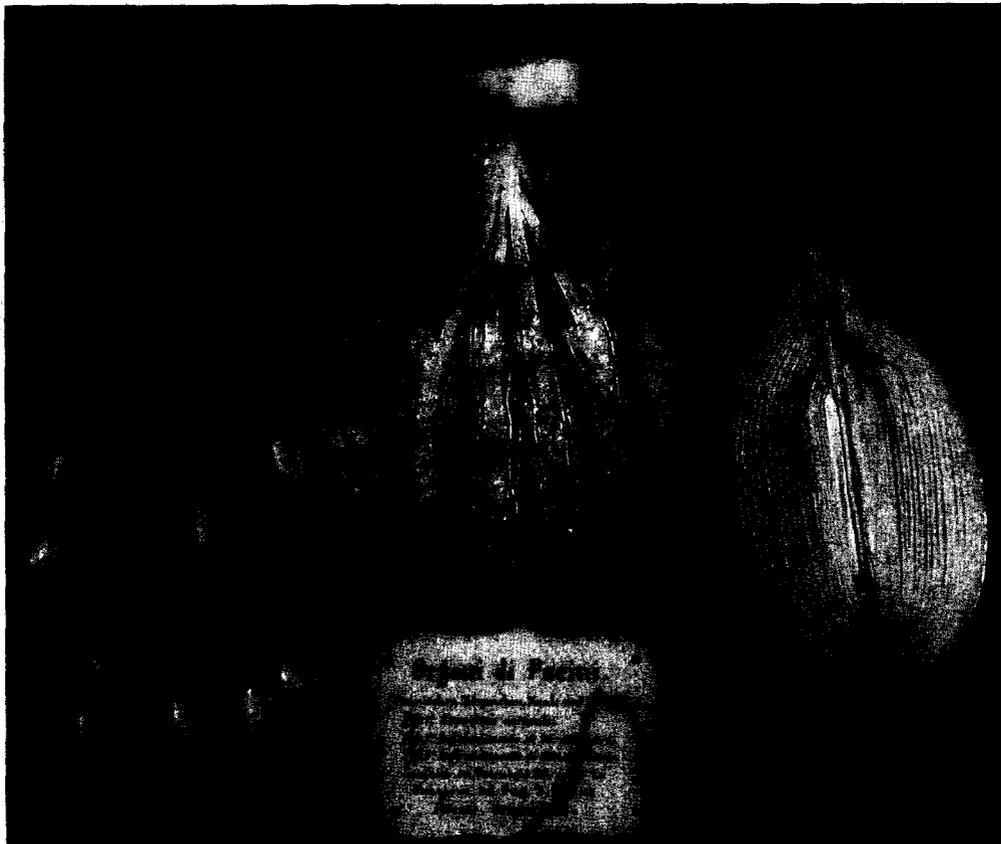


FIG. 3. Wax model of Pacini's organs commissioned by Pacini himself. The hand is "natural size," and two different magnifications of Pacinian corpuscles are shown.

frequency vibrations. The accessory structure, which includes the inner core, intermediate growth zone, outer core, and external capsule (making up 99.9% of the size of the corpuscles) does not play a role in the signal transduction but is involved in the regulation of the ionic environment surrounding the afferent axon and in the mechanical filtering of the stimulus [1].

PACINI AS INNOVATIVE TEACHER AND PASSIONATE MICROSCOPIST

During his university career Pacini introduced (first in Italy) the course of histology and the systematic study of microscopic anatomy in Medical Schools, and was giving practical demonstrations at the microscope during his lectures [6]. His microscope (donated by the philanthrope Niccolò Puccini) was unique in the Faculty. A large collection of letters (kept in the Library of the town hall of Pistoia) to the Dean and Rector of the University and especially to the Grand Duke of Tuscany, Leopold II, documents that Pacini had been fighting for years to obtain microscopes for his students. The Grand Duke initially did not pay much attention to Pacini's requests and received him in a great hurry, impatient to go hunting. However, persuaded by Pacini's insistence, the Grand Duke finally donated one microscope to the University of Florence in the academic year 1844–1845, recommending to Pacini not to waste too much time with the microscope during his courses [6].

At the end of 1844 Pacini investigated microscopically the retina, and described the *membrana limitans interna* [17]. In his subsequent studies he proposed new histological methods and technical modifications of the microscope. Pacini also favoured the introduction of mathematical models in biological studies, and proposed a new method for artificial respiration [2].

PACINI AND THE DISCOVERY OF THE VIBRIO CHOLERA

During a cholera epidemic in Florence in the summer of 1854, Pacini carried out detailed investigations on the etiology of the disease. He based his studies on the histological examination of the intestinal mucosa of cholera patients, performing the autopsy himself a few hours after their death. During these studies, Pacini

first discovered a bacillus, which he described as a *Vibrio* with a comma-like shape. Pacini pursued his investigations on cholera for about 20 years and published several articles (reviewed in ref. [10]). He provided a thorough description of the destruction of intestinal mucosa during cholera and ascribed this devastating damage to the bacillus he had observed. Pacini clearly stated that this *Vibrio* was the "specific" causative agent of the disease. In addition, Pacini insisted that cholera was contagious [3]. The principle of a *contagium vivum* [9] had already been pointed out by Girolamo Fracastoro (1478–1553), a Veronese fellow student of Nicholas Copernicus (1473–1543) at the University of Padua. However, the idea that cholera was contagious was still under dispute, and Pacini's warnings for severe prevention rules were contradicted by the illustrious clinician Maurizio Bufalini (1787–1875), very influential in Italy at that time.

Pacini's data were ignored by the scientific community. The etiological agent of cholera was rediscovered by Robert Koch (1843–1910) in May 1884 (30 years after Pacini's description and 1 year after his death) and was named *Vibrio cholera Koch*. Thus, Pacini never knew that his observations had been confirmed.

Some of the microscope slides prepared by Pacini for his studies on cholera are still kept in the Department of Anatomy and Histology of the University of Florence (Fig. 4).

LATE RECOGNITION

As reported by Bianchi [2], many scientists honoured Pacini on the occasion of a celebration that was held in Pistoia in 1885, and among those:

Camillo Golgi

Filippo Pacini . . . was one of the first to make anatomical studies using the new avenues opened by the microscope; . . . was one of the first to understand the new horizons provided to anatomy by comparative studies and . . . was one of the first to enrich the microscopic technique with procedures that represent a precious help to researchers, having understood the importance of techniques for the minute investigations.

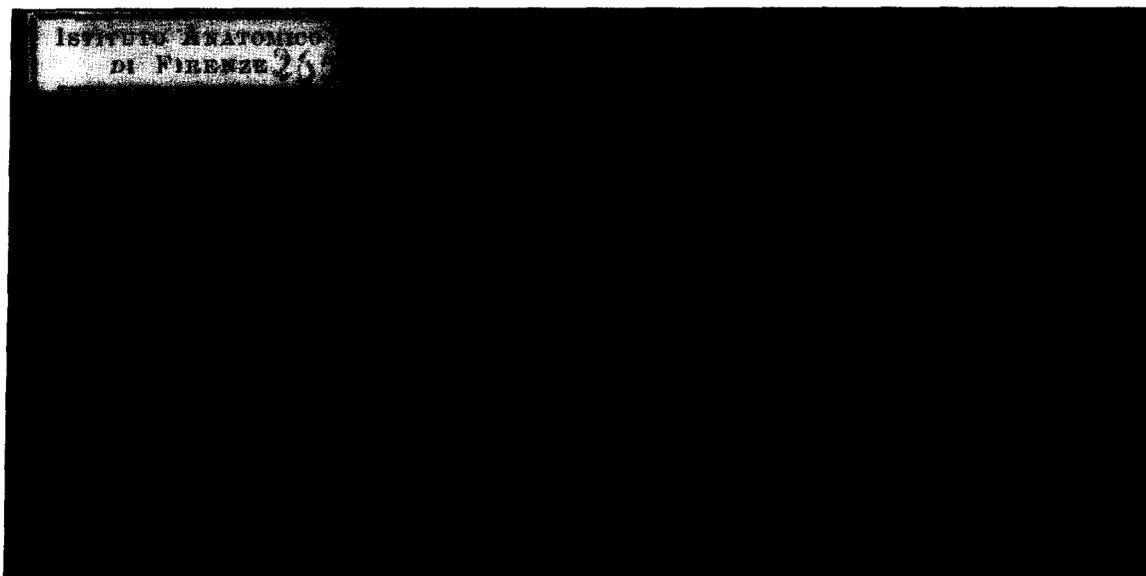


FIG. 4. One of the slides prepared by Pacini from the intestinal mucosa of cholera patients.

Gustav Retzius

Filippo Pacini is one of those men who belong not only to their home land but to the entire world.

Wilhelm Waldeyer

All my admiration to an investigator who, far away from the largest scientific centers, animated by a pure love for science, obtained such important results with the simplest tools.

Wilhelm Krause

I have now been teaching histology at the University of Göttingen for 25 years. When I have to start dealing with nerve terminals I begin with Pacinian corpuscles. And every semester I recall that Pacini, still as a student, with a small nonchromatic microscope and a wooden tube, like those sold at fairs, discovered the corpuscles that are now named after him, which represent the starting point for all that we know nowadays on sensory nerve terminals: you see, gentlemen, it is not the instrument but the observer who makes the discoveries.

REFERENCES

- Bell, J.; Bolanowski, S.; Holmes, M. H. The structure and function of Pacinian corpuscles: A review. *Progr. Neurobiol.* 42:79–128; 1994.
- Bianchi, A. *Relazione e catalogo dei manoscritti di Filippo Pacini*, Florence-Rome: Tipografia Bencini; 1889.
- Castaldi, L. Filippo Pacini nel quarantesimo anniversario della sua morte. *Rivista di Storia delle Scienze Mediche e Naturali* 14:182–212; 1923.
- Cauna, N.; Mannan, G. The structure of human digital Pacinian corpuscles (*Corpuscula lamellosa*) and its functional significance. *J. Anat.* 92:1–25; 1958.
- Coturri, E. Contributo alla storia della divulgazione della scoperta dei corpuscoli del Pacini. *Atti e Memorie dell'Accademia di Storia Sanitaria* 23:1–7; 1957.
- Coturri, E. Un grande anatomico pistoiese dell'Ottocento: Filippo Pacini. *Studi Storici Pistoiesi* 3:35–52; 1978.
- Cruvelhier, J. *Anatomie descriptive*. Paris; 1836.
- Finger, S. *Origin of neuroscience*. New York & Oxford: Oxford University Press; 1994.
- Fracastoro, G. *De sympathia et antipathia rerum liber unus: De contagione et contagiosis morbis et curatione libri tre*. Venice: Eredi Juntae Florentini; 1546.
- Franceschini, P. Filippo Pacini e il colera. *Phisic* 13:324–332; 1971.
- Henle, F.; Kölliker, A. *Ueber die Pacinischen Körperchen an den Nerven des Menschen und der Säugethiere*. Zurich; 1844.
- Key, A.; Retzius, G. *Studien in der Anatomie des Nervensystems und des Bindegewebes*. Stockholm: Samson & Wallin; 1876.
- Lehmann, J. C. *Dissertatio inauguralis medica de consensu partium corporis humani occasione spasmi singularis in manu ejusque digitis ex hernia observati; exposito simul nervorum brachialium et cruralium coailtu peculiari atque papillarum nervearum in digitis dis-positione*. Doctorate Thesis, Vitembergae: Typis Scholmachianis; 1741.
- Mayer, A. F. *Die Pacinischen Körperchen: Eine physiologische Ab-handlung*. Bonn:C. Georgi; 1844.
- Pacini, F. *Sopra un particolare genere di piccoli corpi globosi scoperti nel corpo umano da Filippo Pacini*. Alunno interno degli Spedali riuniti di Pistoia. Letter to the Accademia Medico-Fisica di Firenze; 1835.
- Pacini, F. *Nuovi organi scoperti nel corpo umano*. Pistoia: Tipografia Cino; 1840.
- Pacini, F. *Nuove ricerche microscopiche sulla tessitura intima della retina*. Bologna; 1844.
- Pacini, F. *Osservazioni microscopiche e deduzioni patologiche sul Cholera asiatico*. Florence: Tipografia Bencini; 1854.
- Smith, R. W. *Treatise on the pathology, diagnosis and treatment of neuroma*. Dublin: Hodges and Smith; 1848.
- Thompson, A. J.; Martin, E. A. The Pacinian corpuscle and John Shekleton. *Neurology*, 35:1747; 1985.
- Vater, A. *Dissertatio de consensu patrium corporis humani*. Haller, *Disputationum Anatomicarum selectarum*, Vol. II, Gottingen, 1741:953–972.