normal and deformed spines. Spine 34: 1330-1335, 2009.

28. Southwick WO, Robinson RA: Surgical approaches to the vertebral bodies in the cervical and lumbar regions. J Bone Joint Surg Am 39:631-644, 1957.

29. Tribus CB, Belanger T: The vascular anatomy anterior to the L5-S1 disk space. Spine 26:1205-1208, 2001.

30. Vraney RT, Phillips FM, Wetzel FT, Brustein M: Perideal vascular anatomy of the lower lumbar spine: an endoscopic perspective. Spine 24:2183-2187, 1999.

31. Wood KB, Devine J, Fischer D, Dettori JR, Janssen M: Vascular injury in elective anterior lumbosacral surgery. Spine 35:S66-S75, 2010.

Conflict of interest statement: The authors declare that the article content was composed in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Received 23 July 2011; accepted 29 March 2012

Citation: World Neurosurg. (2013) 79, 5/6:784-791.
http://dx.doi.org/10.1016/j.wneu.2012.03.019

*Journal homepage: **www.WORLDNEUROSURGERY.org***

*Available online: **www.sciencedirect.com***

LEGACY

Iulius Casserius and the First Anatomically Correct Depiction of the *Circulus Arteriosus Cerebri* (of Willis)

Matthew Bender, Alessandro Olivi, Rafael J. Tamargo

Key words
- Anatomy
- Casserius
- Circle of Willis
- *Circulus arteriosus*
- Padua
- Thomas Willis

Abbreviations and Acronyms
ICA: Internal carotid artery
PCA: Posterior cerebral artery
PCoA: Posterior communicating artery
SCA: Superior cerebellar artery


Department of Neurosurgery, The Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

To whom correspondence should be addressed: Rafael J. Tamargo, M.D. [E-mail: rtamarg@jhmi.edu]

Citation: World Neurosurg. (2013) 79, 5/6:791-797.
DOI: 10.1016/j.wneu.2011.10.044

*Journal homepage: **www.WORLDNEUROSURGERY.org***

*Available online: **www.sciencedirect.com***

The *circulus arteriosus cerebri* is the arterial anastomotic circle at the base of the brain, now better known as the circle or polygon of Willis. The British physician and anatomist Thomas Willis (1621-1675) was the first to demonstrate the physiologic function and observe the clinical significance of the *circulus*. It has been overlooked, however, that the first accurate depiction of the *circulus* was provided by the Paduan anatomist Giulio Cesare Casseri (Iulius Casserius) (1552–1616) in two engravings published posthumously in multiple formats, including the *Tabulae anatomicae LXXIIX* (1627). Casserius was the fifth of the six "Vesalian anatomists" at the University of Padua, Italy, which was the site of the most important discoveries in anatomy in the 16th and 17th centuries. Here we review the life of Casserius, his rise from servant to Girolamo Fabrizio D'Acquapendente (Fabricius) (1533–1619) to Professor of Surgery at the University of Padua, his research in comparative anatomy, and his depiction of the *circulus arteriosus cerebri*. Although previous authors have commented on Casserius's portrayal of the *circulus arteriosus* in Table 10 of *Tabulae anatomicae LXXIIX*, none have discussed Figure 2 of Table 9. This is important because whereas the anterior communicating artery complex is depicted clearly in one table, the accurate course of the posterior communicating arteries is shown in the other. Together, Tables 9 and 10 represent a sophisticated, sequential dissection, which deserves recognition as the first accurate portrayal of the arterial anastomosis at the base of the brain.

INTRODUCTION

The *circulus arteriosus cerebri* is the arterial anastomotic circle at the base of the brain that connects the bilateral internal carotid artery (ICA) systems with each other via the anterior communicating artery and also with the vertebrobasilar system via the posterior communicating arteries (PCoAs). Although this structure is common knowledge today, its discovery spanned more than 14 centuries and was the result of a long line of painstaking anatomic research, which started with the description of the *rete mirabile* ("wonderful network") by Aelius Galenus of Pergamum (Galen) (A.D. 129–ca. 202) in his major work entitled *De usu partium* (*On the Usefulness of the Parts*), which he wrote in Greek and finished between A.D. 169 and 175 (9), and culminated in the elucidation of the physiological importance of the *circulus arteriosus* by Thomas Willis (1621–1675), the English anatomist and physician.

Willis and his collaborators described and illustrated this structure in his book *Cerebri anatome: cui accessit nervorum descriptio et usus* (*Anatomy of the Brain and the Description and Use of the Nerves*), published in 1664 (29). Accordingly, the *circulus arteriosus* is now known as the circle or polygon of Willis. Willis initiated his neuroanatomic studies in the new era of anatomic physiology ushered in by William Harvey's (1578–1657) 1628 publication of his landmark treatise on the circulation titled *Exercitatio anatomica de motu cordis et sanguinis in animalibus* (*An Anatomic Exercise on the Motion of the Heart and Blood in Animals*) (12). Harvey, originally

from the town of Folkestone in Kent, England, graduated in 1602 from the University of Padua. He returned to England in 1602 and in 1615–1616 started to lecture at the Royal College of Physicians (25). Harvey advanced the concept that each anatomic structure had a specific function. After Harvey's work, it was no longer sufficient to describe a structure, but instead the challenge was to figure out what was its purpose. Harvey's monumental work on the physiology of the cardiac and peripheral circulation established the foundation for the modern field of physiology and laid the groundwork for Willis's exploration of the physiological implications of the *circulus arteriosus*.

Willis deduced the function of the *circulus arteriosus* based on two experiments and also from clinical observations, which he described in *Cerebri anatome*. In the first experiment, he injected into either carotid artery "a tincture or dyed liquor" and noticed that the entire intracranial vasculature was "imbued with the colour of the same injected liquor." In the second experiment, he injected India ink in one carotid artery and noticed "the tincture or dyed liquor to descend from the other side by the trunk of the opposite Artery" before it came out the jugular veins (29). Finally, drawing from his clinical experience, he described the case of a patient without neurologic deficits who died from a "hard swelling within the Mesentery" and at autopsy was found to have "the right Carotides . . . its cavity being almost wholly shut up; so that the influx of the blood being denied to this passage . . . to wit, the Vertebral Artery of the same side . . . became thrice as big as both Pipes on the other side." He therefore postulated that the vertebral artery compensated for the carotid occlusion (29).

It has been overlooked by those who assign priority in the discovery of the *circulus* to Willis and his collaborator and artist Christopher Wren (1632–1723) (16, 19, 20, 22) that theirs was not the first accurate anatomic depiction of the *circulus arteriosus*. This distinction rightfully belongs to Giulio Cesare Casseri (Iulius Casserius) (1552–1616) (**Figure 1**), the fifth of the six great "Vesalian anatomists" of the University of Padua, who illustrated in detail the *circulus arteriosus* more than 50 years prior to Willis's publication in two engravings published posthumously in 1627. Here we review the life of

Figure 1. Portrait of Giulio Cesare Casseri (Iulius Casserius), from his first publication, *De vocis auditusque organis historia anatomica* (*An Anatomic History on the Organs of Voice and Hearing*) (1600–1601) (4). Reproduced with the permission of Ministero dei Beni e Attività Culturali, Biblioteca Universitaria, Cagliari, Italy.

Casserius and discuss the two plates in which he accurately portrayed the anatomy of the *circulus arteriosus cerebri*.

THE UNIVERSITY OF PADUA AND THE VESALIAN ANATOMISTS

The University of Padua was in the 16th and 17th centuries the site of the most important discoveries in the history of anatomy. In 1543, more than 1300 years after Galen's death, Andreas van Wesel (Vesalius) (1514–1564) published *De humani corporis fabrica libri septem* (*On the Structure of the Human Body in Seven Books*) (28), described by William Osler (1849–1919) as "the greatest book ever printed, from which modern medicine dates" (3). Vesalius, originally from Brussels, arrived in Venice and then moved to Padua in 1536, received his doctorate from the University of Padua on December 5, 1537, and the next day was appointed Professor of Anatomy and Surgery by the faculty of Padua and the Senate of Venice (5). Padua was at the time part of the Venetian Republic, which based its economic strength on free trade with its neighbors and had an open-door policy toward foreigners (5). During the Renaissance, in the same fashion that Florence became the center for art, Padua became the center for science and attracted brilliant students from all over Europe. At the epicenter of the Scientific Revolution was the University of Padua, founded in 1222 by students and faculty who had moved from the University of Bologna. For instance, a contemporary of Casserius at the University of Padua was Galileo di Vincenzo Bonaiuti de' Galilei (Galileo Galilei) (1564–1642), who taught mathematics and astronomy at Padua from 1592 to 1610 (11).

In the *Fabrica*, Vesalius refuted Galen's claim that humans have a *rete mirabile*, an arterial anastomotic connection between branches of the external carotid artery and the cavernous portion of the ICA present in only some mammalian species. He was not, however, the first to notice Galen's error. Jacopo Berengario da Carpi (1460–1530), the surgeon and anatomist of the University of Bologna, first wrote about this in 1521 and in 1522. Based on his dissections, Berengario wrote: "So I believe that Galen has imagined the rete mirabile and he never saw it and I believe that other men after Galen believe in the rete mirabile more because of the opinion of Galen than because of fact" (19). Vesalius did not, however, provide an accurate depiction of the *circulus arteriosus*. The closest he came was to include an illustration of the vasculature on either side of the pituitary gland, which is anatomically inaccurate.

The Venetian Republic, of which Padua was a part, fostered the investigations by Vesalius and his successors through a revolutionary policy requiring cadaveric dissections as part of the medical school curriculum (1). By the time Vesalius left Padua in 1544, after just 7 years as a professor, he had ignited an anatomic revolution that ran its course over about 100 years (1537–1625), which Andrioli and Trincia have named the "Golden Century of Anatomy" (1). Starting with Vesalius, the Chair of Anatomy and Surgery at the University of Padua was occupied by six gifted anatomists who founded the modern science of human anatomy: Vesalius, Realdo Colombo (Columbus) (1516–1559), Gabriele Falloppio (Fallopius) (1523–1563), Girolamo Fabrizio D'Acquapendente (Fabricius) (1533–1619), Giulio Cesare Casseri (Casserius) (1552–1616), and Adriaan van der Spieghel