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History of Medicine

Earliest evidence of malignant breast cancer in Renaissance paintings

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For more on the antiquity of cancer see *PLoS One* 2014; published online March 17. DOI:10.1371/journal.pone.0090924

For more on breast diseases in antiquity see *Quaestiones Medii Aevi Novae* 2014; 19: 103–38; and *Roses DF. Breast Cancer*. Philadelphia, PA: Churchill Livingstone Press, 1999

For more on the case of breast cancer in *La Fornarina* see *Lancet* 2002; 360: 2061–63 and *Lancet* 2003; 361: 1129–30

For more on the previous report of breast cancer in *The Night* see *N Engl J Med* 2000; 343: 1577–78

For more on the history of breast cancer surgery see *J Med Liban* 2009; 57: 65–71 and *Eur J Cancer Care (Engl)* 2009; 18: 530–44

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In the ancient world, breast cancer estimates appear to be higher than those for any other types of cancer. Several potential cases of breast cancer during antiquity have been described in medical papers over the past millennia. However, a clear distinction between breast cancer and other non-malignant breast pathologies cannot be confidently made with the available evidence, and it is not possible to ascertain whether the estimates provided by ancient writers reflect the real incidence of the disease at the time. Indeed, the entire paleopathological history of breast cancer is biased by the fact that sound diagnoses can only be made on the basis of skeletal metastatic

lesions. Similarly, few works of art in antiquity provide clear representations of malignant breast pathologies, but they became more frequent at the beginning of the Renaissance.

A case of breast cancer in the left breast, dated to the 16th century and depicted by Raffaello Sanzio (1483–1520) in *La Fornarina* (Galleria Borghese, Roma; 1518–19), was proposed and challenged, and therefore does not represent a reliable example of breast cancer in Renaissance painting. We present two proposals of the earliest pictorial representations of breast cancer dated to the 16th century: *The Night* (Galleria Colonna, Rome; figure 1) painted by Michele di Rodolfo del Ghirlandaio (1503–77), and *The Allegory of Fortitude* (Galleria dell'Accademia, Florence; figure 2) depicted by Maso da San Friano (1531–71).

The Night (figure 1) is an oil on panel transposition of the homonymous marble-carved statue (1526–31, San Lorenzo Church, Florence; figure 3) sculpted by Michelangelo Buonarroti (1475–1564). A proposed diagnosis of a tumour in the left breast of Michelangelo's statue was previously made on the basis of the abnormal sculpted nipple. However, thanks to the use of different pigments

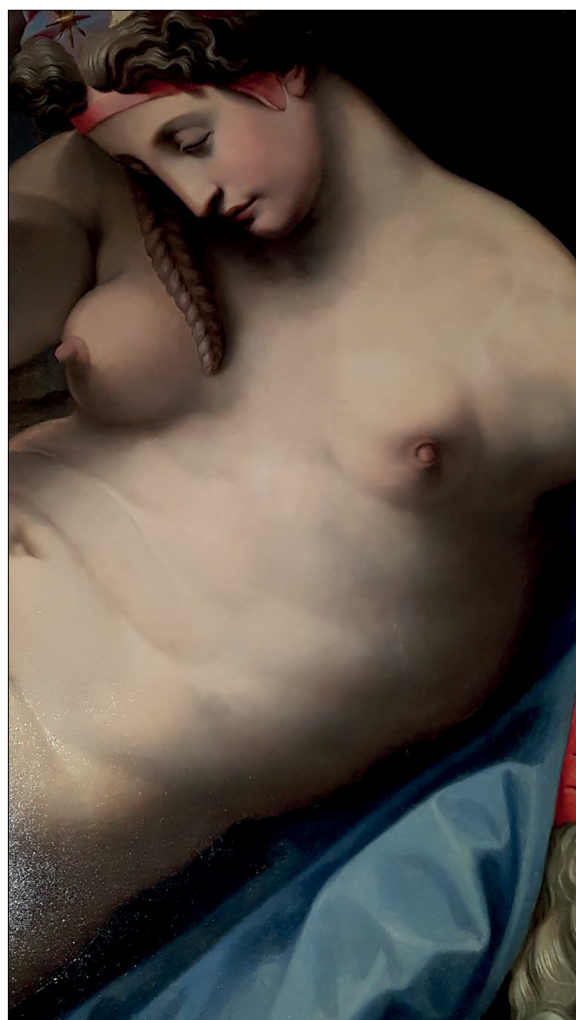


Figure 1: *The Night* by Michele di Rodolfo del Ghirlandaio, oil on panel, 135 × 196 cm, 1555–65, Galleria Colonna, Rome, Italy



Figure 2: *The Allegory of Fortitude* by Maso da San Friano, oil on panel; 178 × 142.5 cm, 1560–62, Galleria dell'Accademia, Florence, Italy

in the painting, further details can be appreciated in the depicted feminine figure, some of which cannot be seen in Michelangelo's statue, and therefore the colour representation helps strengthen the proposed diagnosis. The painting reveals the presence of a large bulge medial to the nipple, an irritated region surrounding the areola-nipple complex, almost complete nipple retraction, and a consistent reduction of the dimension of the entire left breast (figure 1, close-up image). By contrast, only a minimal degree of nipple retraction can be clearly observed in the statue (figure 3, close-up image). The right breast appears to be normal in both representations. On the basis of the details depicted on the canvas, we propose a malignant neoplasia diagnosis in the central region of the left breast with progressive nipple retraction.

In the second case, the feminine figure depicted in *The Allegory of Fortitude* shows an oversized left breast with a large bulge in the lower medial quadrant, a marked erosion of the tip of the nipple, dilated veins, and generalised tumefaction of the areola and of the surrounding skin represented by the characteristic peau d'orange (figure 2). Three small, round-shaped ulcerations underneath the areola-nipple region, and two bigger ulcerations on the medial-lower side of the breast, are also visible (figure 2, close-up image). Moreover, the upper lateral quadrant of the left breast and the armpit are darkened, displaying dilated veins and tumefaction, which could imply that the axillary lymph nodes are affected by the presence of a tumour. These features are consistent with those of an ulcerated, necrotising breast cancer and associated lymphoedema.

The management of breast cancer has evolved slowly throughout the millennia. During antiquity and the Middle Ages, when medicine was dominated by the Hippocratic and Galenic humoral theory, breast cancer and other types of neoplasms were considered to be caused by an excess of black bile. Because of the lack of knowledge about the disease, and its potential to spread and grow in other organs of the body, attempts to treat neoplasias were ineffective.

The Renaissance represented a revolutionary period for medical practice. Universities flourished throughout Europe and scholars started the scientific study of medicine. Dissections enabled knowledge to be gained about human anatomy, and Galen's animal-based anatomical model was finally rejected. The anatomical concept of disease was established, and this was reflected in the therapeutic approaches used. Additionally, advancements in breast tumor surgery were achieved in the 16th century. While the renowned surgeon Ambroise Paré (1510–90) was conservative in the treatment of advanced cancer, his



Figure 3: *The Night* by Michelangelo Buonarroti, marble carved statue; 1526–31, Sacrestia Nuova, San Lorenzo Church, Florence, Italy

pupil, Barthélémy Cabrol (1529–1603), first surgeon of King Henry IV and professor at Montpellier University, recommended mastectomy, including the removal of the pectoralis muscle and the axillary lymph nodes that appeared to be affected by the disease. His approach paved the way to “radical mastectomy” that William R Halsted (1852–1922) would perform three centuries later (1894) in strict aseptic conditions using the newly discovered anaesthetics. However, despite the opportunity to resort to pioneering surgical techniques, radical mastectomy was not commonly practiced during the Renaissance. The lack of general anaesthesia, absence of aseptic techniques, complications derived from wound infection, and postoperative pain and bleeding represented major hurdles for surgeons. Particularly because the breast was, and remains, a symbol of femininity, fertility, and beauty, mastectomy was considered an inhumane practice by Renaissance standards, and therapeutic nihilism prevailed among the vast majority of Renaissance surgeons, resulting in high numbers of visible, advanced breast cancers. We surmise that the depiction of malignant breast cancer in early and late Renaissance works of art was intentional, and possibly reflects a commonly observed female pathological condition of the time.

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