# MAINTAINING GOOD PRACTICE IN BREAST **CANCER MANAGEMENT AND REDUCING** THE CARBON FOOTPRINT OF CARE: STUDY PROTOCOL AND PRELIMINARY RESULTS

M. MATERAZZO<sup>1</sup>, A. FACCHINI<sup>2</sup>, D. GAROZZO<sup>3</sup>, C. BUONOMO<sup>4</sup>, M. PELLICCIARO<sup>1</sup>, G. VANNI1

Abstract - Objective: Health care accounts for up to 8-10% of greenhouse emission yearly in the US and surgical room contributes an estimated 25-30% of hospital waste. Despite the major role of greenhouse emissions because of surgery, little has been done by surgeons to reduce their impact. In this paper, we present a multicentric retrospective analysis to evaluate the carbon footprint of the most common breast surgical treatment and a preliminary analysis of our results.

Patients and Methods: Retrospective analysis with processed-based life cycle assessment (LCA) has been obtained to determine carbon footprint of different surgical procedures. In our preliminary study, we enrolled all consecutive patients undergoing breast conserving procedure (BCP) between 9th March 2019 and 9th March 2021 to underline the reduction in fuel consumption with postoperative telehealth application (pre-COVID-19 vs. COVID-19). A propensity score matching (PSM) was implemented to optimize comparability.

Results: From 276 BCP patients, PSM included 69 pre-COVID-19 and 69 COVID-19 groups, respectively. No statistically significant difference was found in the tumor stage, marital status, and distance from the hospital. A total of 466 postoperative visits was performed and a statistically significant difference in telehealth visit rate was found between groups (1.75% vs. 51.68%; p<0.001). A reduction of 4312.38 km in travel to the hospital was found in the COVID-19 group. No difference was found in postoperative complications.

**Conclusions:** Health systems worldwide are implementing zero-carbon programs to reduce their carbon footprint. Breast surgeons should consider the consequences of their actions and embrace the pillars of the circular economy. Our data could promote further action in order to raise awareness regarding carbon footprint of breast surgery.

**KEYWORDS:** Awake breast surgery, Breast cancer, Breast cancer treatment, Breast Surgery, Carbon footprint, COVID-19.



○ ① S ② This work is licensed under a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International License

DOI: 10.32113/wcrj\_202211\_2438

Department of Surgical Science, Breast Unit, Policlinico Tor Vergata University, Rome, Italy

<sup>&</sup>lt;sup>2</sup>Department of Precision Medicine, University of Study of Campania "L. Vanvitelli", Naples, Italy

<sup>&</sup>lt;sup>3</sup>Department of Clinical Science and Translational Medicine and School of Sports Medicine, University Tor Vergata, Rome, Italy

<sup>&</sup>lt;sup>4</sup>Department of Emergency and Admission, Critical Care Medicine, Pain Medicine and Anesthetic Science, University Tor Vergata, Rome, Italy



# **World Canc**er **Res**earch **J**ournal

### **INTRODUCTION**

COVID-19 disease, declared a pandemic in march 2020, emerged as a novel disease and has remained an unexpected stressor for healthcare systems around the world over the last two years<sup>1,2</sup>.

During the first wave, lockdown measures were designed to reduce COVID-19 infections, hospitalization and deaths<sup>3,4</sup>. During the lockdown, screening and elective activities were suspended, and resources were reallocated to essential services due to the high mortality in frail patients, which consists in elderly, oncological, and transplant patients<sup>5-8</sup>. As a consequence, due to the cessation of all elective activities and the fear of infections, a reduction in elective surgery and breast cancer (BC) treatment was reported<sup>9</sup>.

Breast malignancy has a global prevalence of 2 million<sup>10</sup>. During the lockdown, the arrest of mammographic screening could have resulted in a negative effect on clinical outcomes and cancer care<sup>3,4</sup>. To mitigate these consequences as much as possible, physicians designed temporary measures to continue the surgical and clinical activity during the pandemic and reduce the risk of delayed diagnosis and treatment and introducing innovative technologies and protocols which were still under investigation<sup>11-15</sup>.

Cross-infection reduction with telehealth applications and awake surgery to promote faster discharge were the larger measures of these temporary guidelines before the introduction of COVID-19 vaccine<sup>11,16</sup>. In addition to the health care outcomes, these measures provided a reduction in the private transport toward the hospital, reducing greenhouse gas emission as a secondary, unintended effect<sup>11</sup>. For instance, telehealth applications on postoperative outpatients visit reduced private transportation<sup>5</sup>, and faster discharge and surgery without anesthetic drugs reduced carbon footprint of BC care<sup>17</sup>.

It is well documented that the lockdown positively impacted the environment through the reduction of the emission of greenhouse gases and other pollutants below the pre-COVID-19 levels<sup>18</sup>. Regarding greenhouse emissions, hospital and surgical rooms represent the major sources of pollution. Health care accounts for up to 8-10% of greenhouse emission yearly in the US and surgical room contributes an estimated 25-30% of hospital waste<sup>19</sup>. Several authors are implementing alternative measures to reduce as much as possible the carbon footprint of their treatment, but little has been done in surgery<sup>20</sup>.

Despite the major role of greenhouse emission as a consequence of surgery, little has been done by surgeons to actively reduce their impact on the environment. Our study aims to evaluate the carbon footprint of the most common breast surgical treatment.

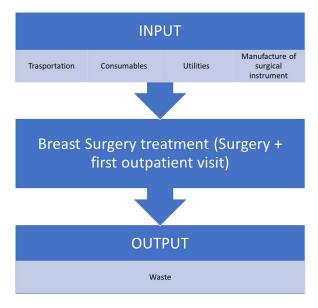
# **PATIENTS AND METHODS**

# Study Design and research questions

The green surgery study aimed to evaluate the carbon footprint of breast surgery. Retrospective analysis of patients with BC will be obtained from clinical records and telephone follow up. Data from the participating institution will be used to assess the following outcomes:

- 1. Determine the carbon footprint of breast conserving procedure;
- 2. Determine the carbon foot print of mastectomy and implant based immediate breast reconstruction<sup>21</sup>;
- 3. Determine the carbon footprint of mastectomy and autologous single stage breast reconstruction .

Processed based life cycle assessment (LCA), a commonly used analysis to determine the environmental impact of all stages of the life cycle of a product, process or service, will be used to assess the carbon footprint of the single procedure. Process-based LCAs measures all material inputs along with emissions of multiple processes which are required to create a final service or product (Figure 1). The final service/product was defined as breast surgery management beginning with the admission onto the surgical ward of each patient before surgery, length of stay, operating room pathway, discharge, and first postoperative visit. Life cycle inventory was defined as all the environmental inputs and outputs of our breast procedure. In our analysis life cycle inventory will be divided as follows: transportation, utilities, hospital consumables, surgical instruments and consumables, sterilization, repacking, and waste.



**Fig. 1.** Processed based Life cycle assessment (LCA) in surgical procedure.

# Study population

In our retrospective study, we will evaluate all consecutive patients with BC diagnoses referred to participating institutions from 1<sup>st</sup> January 2019 to 31 December 2019. This time frame was chosen to avoid any effect of COVID-19 pandemic on BC care and greenhouse emission. Primary inclusion criteria were the diagnosis of non-metastatic BC patients requiring surgical management regardless of preoperative chemotherapy. Other inclusion criteria were age between 18 and 80 years, female sex, and no history of breast surgery.

# Eligible Site

All Italian-certified breast units can participate in the study. In Italy Breast Units are Breast Care Centers designed by National Health System according to EUSOMA guideline<sup>22,23</sup>. Breast Units deliver better outcomes for patients and represent the modern standard in BC care<sup>24</sup>.

After formal Ethics Committee approval, every center will have a site lead (SL) and one or more co-investigator will be required in a local study team. Every SL will be responsible for data collection and entry to facilitate every step of the study.

### **Data Collection**

Data collection will be performed with REDCap web application, a secure software platform designed for data collection<sup>25</sup>. The SL will receive access to the web application after local committee approval. A unique REDCap identifier will be allocated to each patient, and it will be used in correspondence between the study office and participating site.

Data collection will include patient demographics, BC characteristics, and surgical proce-

dure variables as shown in Table 1. Demographic data include patients' age, comorbidities, distance from the hospital, length of stay, and transportation to the hospital. BC characteristics include histological subtype, tumor dimensions, nodal status, prognostic and predictive factors [ER, PR, Ki67 and human epidermal growth factor receptor 2 expression (HER2)]<sup>26,27</sup>. Pathological staging was based on recommendations from AJCC 2018 (edition VIII) of TMN classification. Tumor Grade was calculated with the Nottingham Histologic Score system (the Elston-Ellis modification of Scarff-Bloom-Richardson grading system). The ER, PR and Ki67 receptors are expressed as a percentage of positive cells in specimens studied through immunohistochemistry. Overexpression of Her2 gene (HER2 SCORE) was evaluated by IHC and by FISH, as according to 2013 ASCO/ CAP recommendation. Consequently, patients are classified as Her2-positive if a score 3+ was obtained with IHC or amplification was demonstrated by FISH. All patients are divided into the following subgroups: Luminal A, Luminal B+, Luminal B-, Her2 Type (Her2), and Triple Negative in concordance with the classification of intrinsic subtypes recommended by the San Gallen International Expert Consensus Report of 2017.

Finally, the surgical procedure data set include operative time in minute, the type of surgical procedure, the anesthetic type, all the surgical consumables used in the surgical procedure, and the surgical drapes utilized (disposable *vs.* reusable).

# Missing data

REDCap database grants all the participating sites access to the data through the entire study period. Any missing or erroneous data can be corrected by study team members. 80% of the data must be completed for participants to be accepted in the analysis.

**TABLE 1.** Description of patient's variables collected in the study.

Demographics and preoperative variables	Breast Cancer characteristic	Surgical procedure	
Age	TMN and Stage	Operative time	
Postcode	ER Expression	Surgical procedure	
Distance from hospital in km	_		
BMI	PR expression	Anesthetic regimen	
Comorbidities (as per CCI)	Ki67 Expression	Surgical instrument	
Smoking status	Her2 Score	Surgical drape	
Days of Hospitalization	Molecular subgroup		
Transportation	Histological classification		
	Tumor dimension		

# <mark>World Canc</mark>er <mark>Res</mark>earch Journal

# Statistical Analysis

Categorical variables will be displayed as total and percentage, whereas continuous variables will be presented as means and standard deviation. Mean values of the population will provide information to calculate the surgical footprint of BC surgical care.

# Preliminary study

In the present manuscript, we present the preliminary results of patients in the postoperative follow up after breast conserving procedure. A retrospective analysis was carried out in our institution. The retrospective cohort study included BC patients with Stage I-III BC who underwent breast conserving procedure between 9th March 2019 and 9th March 2021. The patients who met the criteria outlined above were divided into two groups based on the data of their intervention before and after the application of the national lockdown in Italy (8th March 2020) (pre-COVID-19 and COVID-19 group). All clinical data were collected from a prospective maintained database and all our patients routinely sign informed consent for data analysis. All subjects in the prospectively maintained database provided written informed consent for inclusion in the study. This study was conducted in accordance with the Declaration of Helsinki of 1975 (as revised in 2013), and Ethical review and approval were waived for this study due to the retrospective monocentric design. Using propensity score matching (PSM), a 1:1 matched analysis according to age, sex, preoperative clinical stage, axillary node dissection (yes/no), histological subtype, tumor dimensions, prognostic and predictive factors (ER, PR, Ki67 and HER2 status) has been carried out. Our study aimed to compare the number of postoperative surgical outpatients' visits at one month; the average total distance traveled by the patients to reach the hospital at one month, and the average postoperative complication according to modified Clavien-Dindo classification<sup>28</sup>. All patients who perform telehealth visit in our facility usually perform 15-question Telemedicine Satisfaction Questionnaire (TSQ), already validated in diabetic patients and recently in oncology patients<sup>29</sup>.

# **RESULTS**

From 358 patients who performed surgery in our facility in the time frame, 276 patients who underwent in breast conserving procedure for BC

were included in the study. PSM included 69 pre-COVID-19 and 69 COVID-19 groups. Table 2 displays the study data. Among each group, no statistically significant difference was found in the tumor stage, marital status, and distance from hospital. A total of 466 postoperative visits was performed in our facility (3.37 for each patient). Among groups, a statistically significant difference was found in number of telehealth visit in the two different time frames (1.75% vs. 51.68%; p<0.001), resulting in a reduction of 4312.38 km in total distance traveled. In the COVID-19 group, the mean value of TSQ was 72.4. Despite the higher rate of telehealth application in the COVID-19 group, a similar rate of postoperative complications, which required procedures, were reported (10.14% vs. 7.24%, p=0.545).

### **DISCUSSION**

BC is the leading cause of oncological diagnosis, with more than 2 millions cases calculated each year worldwide<sup>10</sup>. After surgery, patients are routinary re-evaluated in the outpatients clinic to detect any early complications, which eventually delay multidisciplinary treatment<sup>30</sup>. In our clinic, before COVID-19 spread, a meticulous reevaluation was considered mandatory to maintain the complication rate lower.

However, as in other subspecialties, COVID-19 pandemic determined a paradigmatic shift in daily clinical practice in BC, enhancing the application of innovative protocols and reducing the admission in the hospital to reduce crossinfection<sup>31</sup>. For instance, precision oncology promoted novel protocols combining a reduction of side effects and the best treatment care<sup>32-34</sup>. Even radiation oncologists were not immune from this revolution, applying hypo fractionated protocols to obtain a systemic immunomodulating effect reducing the admission in the hospital<sup>35,36</sup>.

In our experience, besides technical innovations, such as awake, radio guided-surgery, and tailored axillary procedure for each patient according to age and tumor biology<sup>17,37-39</sup>, telehealth represented the real paradigmatic change in BC surgical care, promoting easier access to facility, without compromising long-term outcome<sup>40,41</sup>. In fact, in the present analysis we demonstrated how telehealth applications could provide a significant reduction in terms of greenhouse emissions with a significant reduction of access in the hospital without compromising the safety of the patients.

Breast surgeons should consider the consequences of their actions and embrace the pillars of the circular economy, as in other professions. For instance,

**TABLE 2.** Demographic Data variable. All continuous data are reported as mean and standard deviation (SD), categorical data are reported as number and percentage.

Variable	Pre-COVID-19 group N=69	COVID-19 group N=69	p-value
Age	58.25 (12.00)	56.25 (11.15)	0.656
Sex F (%)	69 (100%)	69 (100%)	1.000
Premenopausal status yes (%)	23 (33.33%)	20 (28.98%)	0.581
Tumor stage			
0-I	34 (49.27%)	31 (44.92%)	
II	31 (44.92%)	33 (52.16%)	
III	4 (5.79%)	5 (7.24%)	
Axillary node dissection yes (%)	35 (50.72%)	38 (55.07%)	0.608
Tumor subtype			
Ductal carcinoma	64	63	0.942
Lobular carcinoma	4	6	
Special Type	1	0	
ER	45.70% (31.93)	47.45% (26.56)	0.731
PR	50.59% (27.78)	53.78 (30.30)	0.532
Ki67	34.27 (18.70)	34.94 (17.70)	0.831
Her2 overexpression yes (5)	15 (21.73%)	18 (26.09%)	0.549
Marital status yes (%)	40	43	0.734
Distance from the hospital km	13.42 (6.58)	17.53 (6.25)	0.876
Outpatients' visit			
Physical visit	223 (98.24%)	115 (48.31%)	< 0.001
Telehealth	5 (1.75%)	123 (51.68%)	
Clavien Dindo complication			
>2 yes (%)	7 (10.14%)	5 (7.24%)	0.545
Telemedicine Satisfaction Questionnaire (TSQ)	_	72.4	_

industrial and sustainable platforms were designed to produce extracts rich in polyphenols from vegetable waste<sup>42</sup>. Polyphenols are bioactive compounds found in plants, robust evidence demonstrates their beneficial effects on frail patients<sup>43-46</sup>, and production from vegetable waste could reduce the detrimental effect of increase in their demand. Breast surgeons should be aware health systems worldwide are implementing (e.g. delivering a net zero NHS by England NHS) zero-carbon programs to reduce their carbon footprint<sup>47</sup>.

## **CONCLUSIONS**

Physicians and surgeons, as leaders in the health care systems, should promote awareness of climate change and act as key players to reduce as much as possible the impact of health care on climate change. BC, the most common malignancy worldwide, could represent a good study model.

A carbon net zero health system is mandatory to reduce as much as possible the negative effects of climate change on disease and mortality<sup>48</sup>. In the future, clinical trials should assess the carbon

footprint of different measures in order to improve the sustainability of the health care systems. Our further study will focus on awareness in breast surgery regarding carbon footprint of breast clinical practice.

### **ACKNOWLEDGEMENTS:**

None.

# Funding:

None.

### **AUTHORS' CONTRIBUTIONS:**

Study conception and design: Marco Materazzo, Gianluca Vanni. Drafting of article: Marco Materazzo, Marco Pellicciaro. Critical revision: Chiara Buonomo, Daniele Garozzo, Arianna Facchini. Critical revision of literature: Daniele Garozzo, Chiara Buonomo, Arianna Facchini.

All the Authors read and approved the final version of the manuscript.

## **ORCID ID:**

Marco Materazzo: 0000-0002-3599-061X Marco Pellicciaro: 0000-0001-9557-2850 Gianluca Vanni: 0000-0002-3006-5855



# World Cancer Research Journal

#### CONFLICTS OF INTEREST:

The authors declare that they have no conflict of interest to disclose.

#### DATA AVAILABILITY STATEMENT:

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

#### **REFERENCES**

- Vanni G, Pellicciaro M, Materazzo M, Palombi L, Buonomo OC. Breast Cancer Diagnosis in Coronavirus-Era: Alert From Italy. Front Oncol 2020; 10: 938.
- Guarneri C, Rullo EV, Pavone P, Berretta M, Ceccarelli M, Natale A, Nunnari G. Silent COVID-19: what your skin can reveal. Lancet Infect Dis 2021; 21: 24-25.
- 3. Oldani C, Vanni G, Buonomo OC. COVID-19 Unintended Effects on Breast Cancer in Italy After the Great Lockdown. Front Public Health 2020; 8: 601748.
- Vanni G, Pellicciaro M, Materazzo M, Bruno V, Oldani C, Pistolese CA, Buonomo C, Caspi J, Gualtieri P, Chiaravalloti A, Palombi L, Piccione E, Buonomo OC Lockdown of Breast Cancer Screening for COVID-19: Possible Scenario. In Vivo 2020; 34: 3047-3053.
- Vanni G, Materazzo M, Pellicciaro M, Caspi J, Capacci A, Merra G, Capaci A, Merra G. Access to health care after COVID-19 pandemic: is it time for Telemedicine? Eur Rev Med Pharmacol Sci 2020; 24: 9778-9779.
- Calcaterra G, Bassareo PP, Barillà F, Sergi D, Chiocchi M, Romeo F, Mehta JL. The Deadly Quartet (Covid-19, Old Age, Lung Disease, and Heart Failure) Explains Why Coronavirus-Related Mortality in Northern Italy Was So High. Curr Cardiol Rev 2020; 17: 74-77.
- 7. Framarino-Dei-Malatesta M, Derme M, Manzia TM, laria G, De Luca L, Fazzolari L, Napoli A, Berloco P, Patel T, Orlando G, Tisone G. Impact of mTOR-I on fertility and pregnancy: state of the art and review of the literature. Expert Rev Clin Immunol 2013; 9: 781-789.
- Manzia TM, Angelico R, Gazia C, Lenci I, Milana M, Ademoyero OT, Pedini D, Toti L, Spada M, Tisone G, Baiocchi L. De novo malignancies after liver transplantation: The effect of immunosuppression-personal data and review of literature. World J Gastroenterol 2019; 25: 5356.
- Vanni G, Legramante JM, Pellicciaro M, DE Carolis G, Cotesta M, Materazzo M, Buonomo C, Farinaccio A, Santori F, Saraceno F, Ielpo B, Aiello F, Paganelli C, Grande M, DE Andreis G, Chiocchi M, Palombi L, Buonomo OC. Effect of Lockdown in Surgical Emergency Accesses: Experience of a COVID-19 Hospital. In Vivo 2020; 34: 3033-3038.
- Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin 2021; 71: 209-249.
- Buonomo OC, Materazzo M, Pellicciaro M, Caspi J, Piccione E, Vanni G. Tor vergata university-hospital in the beginning of COVID-19-era: Experience and recommendation for breast cancer patients. In Vivo 2020; 34: 1661-1665.
- Vanni G, Pellicciaro M, Materazzo M, Pedini D, Portarena I, Buonomo C, Perretta T, Rizza S, Pistolese C, Buonomo O. Advanced Stages and Increased Need for Adjuvant Treatments in Breast Cancer Patients: The Effect of the One-year COVID-19 Pandemic. Anticancer Res 2021; 41: 2689-2696.

- 13. Hirschfeld CB, Shaw LJ, Williams MC, Lahey R, Villines TC, Dorbala S, et al. Impact of COVID-19 on Cardiovascular Testing in the United States Versus the Rest of the World. JACC Cardiovasc Imaging 2021; 14: 1787.
- Peloso A, Katari R, Murphy S V., Zambon JP, Defrancesco A, Farney AC, Rogers J, Stratta RJ, Manzia TM, Orlando G. Prospect for kidney bioengineering: short-comings of the status quo. Expert Opin Biol Ther 2015; 15: 547-558
- Tariciotti L, D'Ugo S, Manzia TM, Tognoni V, Sica G, Gentileschi P, Tisone G. Combined liver transplantation and sleeve gastrectomy for end-stage liver disease in a bariatric patient: First European case-report. Int J Surg Case Rep 2020; 28: 38-41.
- Mauriello A, Scimeca M, Amelio I, Massoud R, Novelli A, Di Lorenzo F, Finocchiaro S, Cimino C, Telesca R, Chiocchi M, Sun Q, Wang Y, Shi Y, Novelli G, Melino G. Thromboembolism after COVID-19 vaccine in patients with preexisting thrombocytopenia. Cell Death Dis 2021; 12: 762.
- 17. Vanni G, Pellicciaro M, Materazzo M, Dauri M, D'angelillo RM, Buonomo C, De Majo A, Pistolese C, Portarena I, Mauriello A, Servadei F, Giacobbi E, Chiaravalloti A, Buonomo OC. Awake breast cancer surgery: strategy in the beginning of COVID-19 emergency. Breast Cancer 2020; 1: 3.
- 18. Rita E, Chizoo E, Cyril US. Sustaining COVID-19 pandemic lockdown era air pollution impact through utilization of more renewable energy resources. Heliyon 2021; 7: e07455.
- 19. Vacharathit V, Walsh RM, Utech J, Asfaw SH. Action in Healthcare Sustainability is a Surgical Imperative: This is a Novel Way to Do It. J Surg Educ 2021; 79: 275-278.
- 20. Noce A, Di Lauro M, Di Daniele F, Zaitseva AP, Marrone G, Borboni P, Di Daniele N. Natural Bioactive Compounds Useful in Clinical Management of Metabolic Syndrome. Nutrients 2021; 13: 1-37.
- Trapani F, Materazzo M, Petrella G, Vanni G, Orsaria P, Genova F, Granai A V, Pistilli G, Portarena I, Buonomo OC. One-time (OTR) or double-time (DTR) breast reconstruction: Oncological aspects and quality of life. Eur J Cancer 2018; 92: S82.
- Biganzoli L, Marotti L, Cardoso MJ, Cataliotti L, Curigliano G, Cuzick J, Goldhirsch A, Leidenius M, Mansel R, Markopoulos C, Wyld L, Rubio IT. European guidelines on the organisation of breast centres and voluntary certification processes. Breast Care 2019; 14: 359-365.
- Pistolese CA, Lamacchia F, Tosti D, Anemona L, Ricci F, Censi M, Materazzo M, Vanni G, Collura A, Di Giuliano F, Perretta T, Buonomo OC. Reducing the Number of Unnecessary Percutaneous Biopsies: The Role of Second Opinion by Expert Breast Center Radiologists. Anticancer Res 2020; 40: 939-950.
- Kesson EM, Allardice GM, George WD, Burns HJG, Morrison DS. Effects of multidisciplinary team working on breast cancer survival: Retrospective, comparative, interventional cohort study of 13 722 women. BMJ 2012; 344: e2718.
- Harris PA, Taylor R, Minor BL, Elliott V, Fernandez M, O'Neal L, McLeod L, Delacqua G, Delacqua F, Kirby J, Duda SN. The REDCap consortium: Building an international community of software platform partners. J Biomed Inform 2019; 95: 103208.
- Buonomo OC, Grasso A, Pistolese CA, Anemona L, Portarena I, Meucci R, Morando L, Deiana C, Materazzo M, Vanni G. Evaluation of Concordance Between Histopathological, Radiological and Biomolecular Variables in Breast Cancer Neoadjuvant Treatment. Anticancer Res 2020; 40: 281-286.

- Orsaria P, Caredda E, Genova F, Materazzo M, Capuano I, Vanni G, Granai AV, de Majo A, Portarena I, Sileri P, Petrella G, Palombi L, Buonomo OC. Additional nodal disease prediction in breast cancer with sentinel lymph node metastasis based on clinicopathological features. Anticancer Res 2018; 38: 2109-2117.
- Panhofer P, Ferenc V, Schütz M, Gleiss A, Dubsky P, Jakesz R, Gnant M, Fitzal F. Standardization of morbidity assessment in breast cancer surgery using the Clavien Dindo Classification. Int J Surg 2014; 12: 334-339.
- Poinsot R, Altmeyer A, Conroy T, Savignoni A, Asselain B, Léonard I, Marx E, Cosquer M, Sévellec M, Gledhill J, Rodary C, Mercier M, Dickès P, Fabbro M, Antoine P, Guerif S, Schraub S, Dolbeault S, Brédart A. [Multisite validation study of questionnaire assessing out-patient satisfaction with care questionnaire in ambulatory chemotherapy or radiotherapy treatment]. Bull Cancer 2006; 93: 315-327
- 30. Kontos M, Markopoulos C. Complications of Breast Surgery and Their Management. Breast Cancer Manag Surg 2018: 411-423.
- 31. Omranipour R, Mahmoodzadeh H, Hadjilooei F, Alipour S. Recommendations for breast surgical care during COVID-19 outbreak in Iran: setting priorities of management. World Cancer Res J 2020; 7: e1588.
- 32. Dimitrov G, Atanasova M, Popova Y, Vasileva K, Milusheva Y, Troianova P. Molecular and genetic subtyping of breast cancer: the era of precision oncology. World Cancer Res J 2022; 9: e2367.
- 33. Caputo R, Cianniello D, Giordano A, Piezzo M, Riemma M, Trovò M, Berretta M, De Laurentiis M. Gene Expression Assay in the Management of Early Breast Cancer. Curr Med Chem 2020; 27: 2826-2839.
- 34. Roselli M, Guadagni F, Buonomo O, Belardi A, Ferroni P, Diodati A, Anselmi D, Cipriani C, Casciani CU, Greiner J, Schlom J. Tumor markers as targets for selective diagnostic and therapeutic procedures. Anticancer Res 1996; 16: 2187-2192.
- 35. Muraro E, Furlan C, Avanzo M, Martorelli D, Comaro E, Rizzo A, Fae' DA, Berretta M, Militello L, Del Conte A, Spazzapan S, Dolcetti R, Trovo' M. Local high-dose radiotherapy induces systemic immunomodulating effects of potential therapeutic relevance in oligometastatic breast cancer. Front Immunol 2017; 8: 1476.
- Franco RDI, Borzillo V, D'Ippolito E, Scipilliti E, Petito A, Facchini G, Berretta M, Muto P. COVID-19 and radiotherapy: Potential new strategies for patients management with hypofractionation and telemedicine. Eur Rev Med Pharmacol Sci 2020; 24: 12480-12489.
- 37. Buonomo O, Cabassi A, Guadagni F, Piazza A, Felici A, Piccirillo R, Atzei GP, Cipriani C, Schiaroli S, Mariotti S, Guazzaroni MN, Cossu E, Simonetti G, Pernazza E, Casciani CU, Roselli M. Radioguided-surgery of early breast lesions. Anticancer Res 2001; 21: 2091-2097

- 38. Orsaria P, Varvaras D, Vanni G, Pagnani G, Scaggiante J, Frusone F, Granai AV, Petrella G, Buonomo OC. Nodal Status Assessment in Breast Cancer: Strategies of Clinical Grounds and Quality of Life Implications. Int J Breast Cancer 2014; 2014: 469803.
- 39. Vanni G, Materazzo M, Pellicciaro M, Morando L, Portarena I, Anemona L, D'Angelillo RM, Barbarino R, Chiaravalloti A, Meucci R, Perretta T, Deiana C, Orsaria P, Caspi J, Pistolese CA, Buonomo OC. Does Age Matter? Estimating Risks of Locoregional Recurrence After Breast-conservative Surgery. In Vivo 2020; 34: 1125-1132.
- 40. Dietze EC, Sistrunk C, Miranda-Carboni G, O'Regan R, Seewaldt VL. Triple-negative breast cancer in African-American women: Disparities versus biology. Nat Rev Cancer 2015; 15: 248-254.
- Vanni G, Tazzioli G, Pellicciaro M, Materazzo M, Paolo O, Cattadori F, Combi F, Papi S, Pistolese CA, Cotesta M, Santori F, Caspi J, Chiaravalloti A, Muscoli S, Lombardo V, Grasso A, Caggiati L, Raselli R, Palli D, Altomare V, D'Angelillo RM, Palombi L, Buonomo OC. Delay in Breast Cancer Treatments During the First COVID-19 Lockdown. A Multicentric Analysis of 432 Patients. Anticancer Res 2020; 40: 7119-7125.
- 42. Romani A, Campo M, Urciuoli S, Marrone G, Noce A, Bernini R. An Industrial and Sustainable Platform for the Production of Bioactive Micronized Powders and Extracts Enriched in Polyphenols From Olea europaea L. and Vitis vinifera L. Wastes. Front Nutr 2020; 7: 120.
- 43. Merra G, Noce A, Marrone G, Cintoni M, Tarsitano MG, Capacci A, De Lorenzo A. Influence of Mediterranean Diet on Human Gut Microbiota. Nutrients 2020; 13: 1-12
- 44. Romani A, Bernini R, Noce A, Urciuoli S, Lauro M Di, Zaitseva AP, Marrone G, Di Daniele N. Potential Beneficial Effects of Extra Virgin Olive Oils Characterized by High Content in Minor Polar Compounds in Nephropathic Patients: A Pilot Study. Molecules 2020; 25: 4757.
- Noce A, Marrone G, Di Lauro M, Urciuoli S, Pietroboni Zaitseva A, Wilson Jones G, Di Daniele N, Romani A. Cardiovascular Protection of Nephropathic Male Patients by Oral Food Supplements. Cardiovasc Ther 2020; 2020: 1807941.
- 46. Tinti F, Lai S, Noce A, Rotondi S, Marrone G, Mazzaferro S, Di Daniele N, Mitterhofer AP. Chronic Kidney Disease as a Systemic Inflammatory Syndrome: Update on Mechanisms Involved and Potential Treatment. Life 2021; 11: 419.
- 47. National Health System Delivering a "Net Zero" National Health Service "https://www.england.nhs.uk/greenernhs/wp-content/uploads/sites/51/2020/10/delivering-a-net-zero-national-health-service.pdf (accessed november 2, 2022)".
- 48. Calleja-Agius J, England K, Calleja N. The effect of global warming on mortality. Early Hum Dev 2021; 155: 105222.