

Team di ricerca: **PORT** in lung cancer.

The role of adjuvant radiotherapy (PORT) in non-small cell lung cancer: how the techniques can improve cardiopulmonary toxicity.

Work programme

The extent of lymph node involvement in patients affected by stage III NSCLC, undergoing surgery, is a prognostic factor for overall survival.

In pN2 patients it is necessary to proceed with the evaluation of adjuvant radiotherapy treatment. The 1998 PORT (Post-Operative Radio-Therapy) meta-analysis, while demonstrating a negative effect on survival in radically resected stage I-II patients, does not clarify the existence of a clinical benefit in stage III patients. Although some methodological criticisms regarding this meta-analysis are justified (inclusion of predominantly very dated studies, conducted with different total doses, radio-biologically suboptimal fractionation schemes, use of equipment technically unsuitable for thoracic irradiation, treatment volumes and radiotherapy planning not congruent) to date there is no randomized scientific evidence in favor of an adjuvant radiotherapy treatment. In any case, treatment today must include the administration of a total dose between 50-54 Gy, with conventional fractionation (1.8-2 Gy / day), to a target volume represented by the ilo-mediastinal lymph node stations involved in the disease, from the section shear always considering the hilum and the subcarinal station.

The results of the LungART trial, a prospective randomized European study aimed at evaluating the usefulness of adjuvant radiotherapy in patients undergoing radical surgical resection with pathological findings of involvement of the mediastinal lymph node stations (PN2), were presented for the first time at ESMO 2020. The study enrolled 501 patients, demonstrating a non-significant increase in DFS at three years, with a reduction in mediastinal recurrence, in favor of the PORT arm. The fact that seems to affect the absence of advantage in DFS and OS the most is represented by the safety of the treatment. In fact, the study reported mainly higher cardio-pulmonary complication rates in the experimental arm (16.2% vs 2%) as well as an increase in G3-G4 toxicity (23.7% vs 15%), with a death rate of 5.3% in the control arm and 14.6% in the experimental arm, such as not to allow the recommendation of postoperative radiotherapy in all patients operated on in stage IIIA (pN2).

The study presents an important bias, related to the technique (3DCRT) used for the contouring of these patients, now considered obsolete for NSCLC and now replaced by intensity modulated techniques (IMRT / VMAT).

The goal of the research group is to demonstrate how the use of increasingly conformed radiotherapy techniques allows to minimize the risk of acute and late complications, both of the respiratory type and of other organs at risk, such as the heart and the esophagus such as to reduce the known dose constraints.

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Key Networks:

AIRO lung

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Key Publications:

Massafra, R., Bove, S., La Forgia, D., Comes, M. C., Didonna, V., Gatta, G., Narodne, A., ... & Lorusso, V. (2022). An Invasive Disease Event-Free Survival Analysis to Investigate Ki67 Role with Respect to Breast Cancer Patients' Age: A Retrospective Cohort Study. *Cancers*, *14*(9), 2215.

Comes, M. C., Fanizzi, A., Bove, S., Didonna, V., Diotaiuti, S., La Forgia, D., Nardone, A., ... & Massafra, R. (2021). Early prediction of neoadjuvant chemotherapy response by exploiting a transfer learning approach on breast DCE-MRIs. *Scientific Reports*, *11*(1), 1-12.

Guida, M., Bartolomeo, N., De Risi, I., Fucci, L., Armenio, A., Filannino, Nardone, A., R., ... & Strippoli, S. (2019). The management of oligoprogression in the landscape of new therapies for metastatic melanoma. *Cancers*, *11*(10), 1559.

Massafra, R., Bove, S., Lorusso, V., Biafora, A., Comes, M. C., Didonna, V., Nardone, A., ... & La Forgia, D. (2021). Radiomic feature reduction approach to predict breast cancer by contrast-enhanced spectral mammography images. *Diagnostics*, *11*(4), 684.

Massafra, R., Latorre, A., Fanizzi, A., Bellotti, R., Didonna, V., Giotta, F., Nardone, A., ... & Lorusso, V. (2021). A clinical decision support system for predicting invasive breast cancer recurrence: preliminary results. *Frontiers in Oncology*, *11*, 576007.

Fanizzi, A., Lorusso, V., Biafora, A., Bove, S., Comes, M. C., Cristofaro, C., Nardone, A., ... & Massafra, R. (2021). Sentinel lymph node metastasis on clinically negative patients: Preliminary results of a machine learning model based on histopathological features. *Applied Sciences*, *11*(21), 10372.

Strippoli, S., Fanizzi, A., Quaresmini, D., Nardone, A., Armenio, A., Figliuolo, F., ... & Guida, M. (2021). Cemiplimab in an elderly frail population of patients with locally advanced or metastatic cutaneous squamous cell carcinoma. A monocenter real-life experience from Italy. *Frontiers in oncology*, 4481.

Strippoli, S., Fanizzi, A., Negri, A., Quaresmini, D., Nardone, A., Armenio, A., ... & Guida, M. (2021). Examining the Relationship between Circulating CD4⁺ CD8⁻ Double-Negative T Cells and Outcomes of Immuno-Checkpoint Inhibitor Therapy—Looking for Biomarkers and Therapeutic Targets in Metastatic Melanoma. *Cells*, *10*(2), 406.