

in patients treated for left-sided breast cancer without breath-hold were higher when compared to those with right-sided breast cancers and to those with left-sided breast cancer treated with breath-hold. See the Table and the Figure.

Group	Mean CAC LAD_baseline	Mean CAC Overall_baseline	Mean CAC LAD_3 years	Mean CAC Overall_3 years
R (n=20)	14.5 (0-105)	80.1 (0-825)	29.9 (0-255)	138 (0-1334)
L-BH (n=18)	49.3 (0-334)	75.2(0-477)	77.3 (0-634)	138.3 (0-1055)
L+BH (n=61)	19.3 (0-401)	35.7 (0-645)	28.8 (0-509)	64.9 (0-1039)

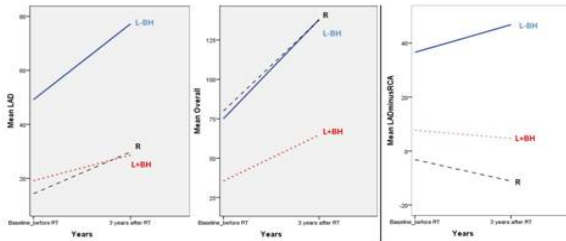


Figure left and middle: Mean calcium score increase in time for the LAD and overall CAC score. Figure right: Mean CAC score: LAD minus RCA.

Blue solid line: Left-sided breast cancer patients, group L-BH. Black dashed line: Right-sided breast cancer patients, group R. Red dotted line: Left-sided breast cancer patients treated in breath-hold, group L+BH. Note: the scales in the figure differ.

Conclusions: Breath-hold in breast conserving radiotherapy leads to a less pronounced increase of CT based CAC scores. Therefore, breath-hold is probably useful to prevent the development of radiation-induced coronary artery disease. The drawbacks of our study were the small numbers and the relatively short follow-up period.

PO-0681

Re-irradiation with hyperthermia for loco-regional recurrent breast cancer: A systematic review and meta-analysis

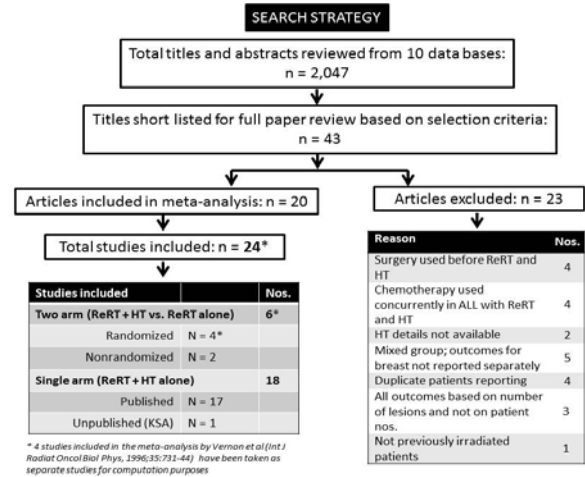
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Purpose/Objective: Loco-regional recurrences in post-irradiated breast cancers pose a major therapeutic challenge and could severely compromise patients' quality of life. Since in most cases, patients usually have co-existing systemic disseminated disease, a sustainable complete local regression of the recurrences, without treatment induced morbidity could provide an effective palliation and improve their quality of life. Local hyperthermia (HT) along with moderate doses of re-irradiation (ReRT) has been used in various single-arm (ReRT+HT) and two-arm clinical trials (randomized and nonrandomized, ReRT vs. ReRT+HT). The present study conducts a systematic review and meta-analysis on the outcome of these trials.

Materials and Methods: Using the appropriate MeSH and Boolean function, a detailed search was conducted as per the PRISMA guidelines. 2,047 abstracts were screened from the 10 databases used for search (Fig). Only those studies which had received prior loco-regional RT as a part of their primary management and were treated with ReRT and HT alone were considered. Patients who had undergone surgery for the loco-regional recurrences were subjected to concurrent chemotherapy were not considered. End point evaluation was complete loco-regional response (CR) following ReRT and HT.



Results: A total of 43 full papers were shortlisted and reviewed after extensive database search, and 24 studies were selected for detailed review based on pre-defined selection criteria. Six of these were two-arm (randomized, n=4; nonrandomized, n=2) while 18 were single-arm studies resulting in a total of 1,319 patients of which 1,162 received ReRT and HT.

Primary RT at doses ranging from 40 to 60 Gy (mean ± SD: 50.6 ± 6.1 Gy) was received by these patients between 37 and 72 months before being considered for ReRT. Hyperthermia was mostly delivered by microwaves (91.7%), twice a week and usually following RT (79.2%). A temperature ranging from 40.6 - 43 °C (42.4 ± 0.7 °C) was achieved during HT which lasted for a mean duration of 53.5 min. ReRT doses ranged from 24 - 60 Gy (36.3 ± 8.1 Gy) and delivered at 1.8 to 4 Gy/fr (2.85 ± 0.9 Gy).

Two-arm studies included 494 patients, and a CR of 62.8% and 39.3% was observed with ReRT+HT and ReRT respectively, giving an odds ratio of 2.9 (95% CI: 1.8-4.6, p<0.001; Q=6.4, I²= 22.2, p=0.26). The risk ratio was 1.6 (95% CI: 1.2-2.0) in favor of achieving a CR with ReRT+HT compared to ReRT alone. For 18 single-arm studies, a CR of 64.6% was reported from the 825 patients resulting in an event rate of 0.6 (95% CI: 0.5-0.6, p<0.001; Q=33.8, I²= 49.7, p=0.008). Local control with ReRT +HT at 1 and 2 year were 57.1% and 48.5% respectively. Mean acute and late grade III/IV toxicities with ReRT +HT were reported as 13.4% and 3.9%.

Conclusions: ReRT with HT substantially increases the probability of achieving CRs in loco-regional recurrences in pre-irradiated patients with low acute and late morbidities.

PO-0682

External validation of the derived neutrophil-to-lymphocyte ratio as a prognostic factor in breast cancer patients

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Purpose/Objective: Existing preclinical and clinical data suggest that the presence of a systemic inflammatory response plays a critical role in the progression of several solid tumors. The derived neutrophil-to-lymphocyte ratio (dNLR) represents an easily determinable marker of systemic inflammation and has been proposed as a potential prognostic marker. The present study was performed to externally validate the prognostic relevance of an elevated pre-treatment dNLR in a large cohort of non-metastatic breast cancer patients.

Materials and Methods: Data from 762 consecutive non-metastatic female breast cancer patients treated from 1999 to 2004 were evaluated. Disease-free survival (DFS), distant metastases-free survival (DMFS), and overall survival (OS) were assessed using the Kaplan-Meier method. To evaluate the prognostic relevance, univariate and multivariate Cox regression models were performed for each endpoint.

Results: Applying receiver-operating characteristics (ROC) analysis, the optimal cut-off level for the dNLR was 3. In univariate analysis, a dNLR ≥ 3 was associated with poor DFS (HR 1.87, 95%CI 1.28-2.73, $p=0.001$), DMFS (HR 1.90, 95%CI 1.27-2.85, $p=0.002$), and OS (HR 1.67, 95%CI 1.07-2.63, $p=0.025$). Multivariate analysis revealed a significant association between the elevated dNLR and poor DFS (hazard ratio (HR) 1.70, 95%CI 1.09-2.65, $p=0.018$) and DMFS (HR 1.66, 95%CI 1.02-2.68, $p=0.041$) but did not show a significant association between the dNLR and OS (HR 1.54, 95%CI 0.91-2.59, $p=0.106$).

Conclusions: In the present study, we confirmed the elevated pre-treatment dNLR as an independent prognostic factor that could be useful for future individual risk assessment in breast cancer patients.

PO-0683

Electron IntraOperative RadioTherapy (ELIOT) in early breast cancer: Outcome analysis of a non-randomized study

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Purpose/Objective: Intraoperative radiotherapy (IORT) has been proposed as alternative to external beam in early breast cancer however previous studies suggest that patient selection must be improved in order to reduce the rate of ipsilateral breast tumour recurrence (IBTR). 'Papa Giovanni XXIII' Hospital in Bergamo Italy has been authorized by Lombard Aldermanship to carry out a non-randomised study. The study was also approved by the local ethics committee. **Materials and Methods:** 735 procedures has been performed between February 2006 and June 2014, on 722 patients (mean age 64 years; range 48-84 years), 13 of them had doubled IORT (synchronous or metachronous). Patients inclusion/exclusion criteria were: Age > 48 years old (if postmenopausal); clinical, mammography/ultrasound diagnostic of unifocal invasive carcinoma with an ultrasound major diameter < 2.5 cm. Informed consent was mandatory. There were 41 protocol violations due the age or the nodule size, enclosed in the analysis.

IORT was done by means of a 9 MeV electron beam Novac 7 linac. The prescribed dose was 21 Gy at 90 % isodose. The mean follow up is 1564 days and all patients with at least one follow up are enclosed in the analysis. The principal endpoint was the in-field and out-field (IBTR), Relapse Free Survival (RFS). The secondary endpoints were the Overall Survival (OS), Cancer Specific Survival (CSS), Metastases Free Survival (MFS), Disease Free Survival (DFS) and the acute and late toxicity rates.

Survival dependence on different parameters such as nodule size, ER, PR, focality, grade, vascular invasion, Ki67>20, margins, cErbB2, has been assessed by log-rank test.

Results: Observed local relapses are 52 (33 in field, 17 out-field, 2 n.o.s.), corresponding to a crude rate of 7.1 % the 5 years cumulative RFS, DFS, MFS were 92.1%, 89% and 94.7% respectively. The 5 years OS and CSS were 98.8% and 99.4% respectively.

The univariate statistical analysis showed that IBTR dependence on the independent variables: nodule size, ER, PR, focality, grade, vascular invasion, Ki67>20, margins, cErbB2 was statistically significant. Dependence on the other variables such as DCIS component, histological type, pN, showed a trend but is not statistically significant. This last result may be due to the dimension of subgroups. Concerning nodule dimension, the most significant difference in IBTR occurs when a cut-off value of 15 mm is used. Grouping the patients according to ASTRO guidelines for accelerated partial breast irradiation, patients scored in the 'suitable' group showed a much better RFS as compared to 'cautionary' or 'unsuitable' group.

