

# Intraoperative Radiation Therapy for Breast Cancer Not Associated with Pulmonary Complications

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## Abstract

Radiation pneumonitis and radiation-induced cryptogenic organizing pneumonia are common complications after external beam radiation therapy following breast conserving surgery for patients with early stage breast cancer. Intraoperative radiation therapy (IORT) is designed to decrease radiation exposure to the lung, skin, soft tissue, and contralateral breast. A single-center, retrospective cohort of all patients receiving IORT between 2009 and 2013 was analyzed, and 122 cases of IORT were found. There were no instances of pulmonary complication in patients receiving IORT without whole breast irradiation. The only instance of radiation pneumonitis identified was in a patient who received subsequent external beam radiation after boost IORT. As there are no previous systemic evaluations of pulmonary complications of IORT, this study supports its reported safety.

**Keywords:** Breast cancer; Breast conserving surgery; Intraoperative radiation therapy; Radiation pneumonitis

## Introduction

Breast conserving surgery with breast irradiation has been the standard surgical treatment for early stage breast cancer for decades. Long-term survival rates of this procedure are similar compared to radical and modified radical mastectomy [1,2]. Without breast irradiation, breast conserving therapy alone leads to increased risk or recurrence [3]. Radiation therapy is associated with a variety of effects, including vascular damage, immunologic effects, and secondary malignancies.

Chief among the pulmonary complications is radiation pneumonitis (RP) and cryptogenic organizing pneumonia (COP). The reported incidence of RP varies, but is typically 5-20 percent. It presents with usual symptoms of cough, dyspnea, and chest tightness 3-8 weeks after radiation (but occasionally up to 6 months). Most cases resolve spontaneously, but some rapidly progress to pulmonary fibrosis and death in 6-12 months. Factors associated with RP include prior radiation, concomitant chemotherapy, endocrine therapy, and withdrawal of steroids [4].

Radiation-induced COP correlates geographically and temporally with RP. Unlike RP, COP occurs independent of the radiation dose and outside the radiation field. RP typically occurs in the periphery in the irradiated lung, while COP can occur outside the radiation field [5].

For nearly 15 years, some patients have been treated with intraoperative radiation therapy (IORT). Patients selected typically have limited breast cancer with a tumor size of less than 2.5 cm. The use of IORT should decrease the exposure of other tissues like skin, soft tissue, heart, and lung to the damaging effects of radiation. When 21 Gy IORT is compared to 50 Gy fractionated external beam radiation therapy (EBRT) there is a 4.8% absolute increased risk of recurrence

but no change in mortality [6]. In those patients at high risk for recurrence, boost IORT with a lower dose can precede EBRT. While fewer adverse events related to the skin occur with IORT,<sup>5</sup> no study has shown the incidence of pulmonary complications of IORT in breast-conserving surgery. Thus the purpose of this investigation was to determine the incidence of pulmonary complications in patients receiving IORT for breast cancer at a single subspecialized cancer hospital.

## Methods and Materials

The study was deemed exempt after review by the hospital's contracted institutional review board, Western Institutional Review Board®. Charts were reviewed retrospectively for all patients receiving intraoperative radiation therapy during breast conserving surgery at Cancer Treatment Centers of America, Eastern Regional Medical Center. Between January 2009 and September 2013, 122 breast IORT treatments in 120 women were identified. No male patients received IORT. The median age for patients was 56 years (range 37 to 83). Table 1 describes the comorbidities of the patient population. The most common pre-existing condition was hypertension (44% of the cohort). Asthma and COPD were represented in 11% and 12% of patients, respectively. Eighteen percent were smokers (Table 1).

	N (%)
Asthma	13 (11%)
COPD	15 (12%)
Coronary disease	3 (2.5%)
Depression	23 (19%)
Diabetes	20 (17%)
Dyslipidemia	30 (25%)

GERD	32 (27%)
Hypertension	53 (44%)
Obesity	15 (13%)
Sarcoidosis	3 (2.5%)
Tobacco use	22 (18%)

**Table 1:** Comorbidities of patients.

All patients received intraoperative radiation with the Novac 7 mobile accelerator. Either an aluminum/lead shield or a copper/lead shield was placed below the breast tissue and above the pectoralis during surgery. A dose of 21 Gy was typically used intraoperative when IORT was anticipated to be the only radiotherapy. For patients at high risk for recurrence, 10 Gy boost IORT was used with additional whole breast radiation. Radiation dose was determined by the radiation oncologist in coordination with medical and surgical oncologists. When appropriate, adjuvant/neoadjuvant chemotherapy was prescribed.

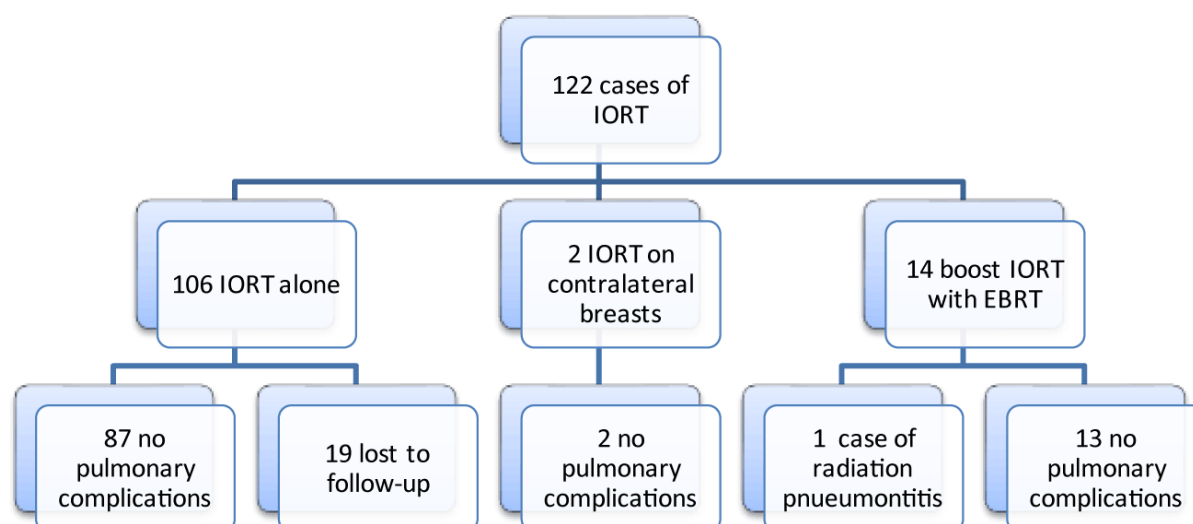
All post-operative billing data was analyzed for the 120 patients during the subsequent 12 months. Radiation pneumonitis and radiation-induced COP (including synonyms like bronchiolitis obliterans organizing pneumonia) were explicitly screened for the review. In addition, signs and symptoms that could be used to describe RP and COP were screened for, including cough, fever, dyspnea, pulmonary fibrosis, pneumonitis, and "respiratory abnormality." When these clues were found, the chart was further reviewed. No extrapolation from charted information was permitted or necessary.

## Results

A total of 120 patients received IORT during the time period reviewed (Figure 1). Of these, 106 patients received IORT alone without additional radiation therapy. 88 had no pulmonary complications after one year, and 18 (16.7% of IORT and bilateral IORT) did not complete 12 month follow-up at the center. The range of follow-up was 1 to 7 months (median 2, mean 2.5 months) without pulmonary complication. Four of these patients expressed desire to transfer care, and the remaining 12 provided no explanation. Two IORT patients had contralateral breast cancer. In both instances, over a year after the first IORT passed without complication before breast cancer was diagnosed on the opposite side. IORT was used on that side with another 12 months of no complications. Of the 14 patients with boost IORT followed by external beam radiation, 13 had no pulmonary complication after one year.

One patient in this cohort developed radiation pneumonitis. She was a 53 year old with a history of hypothyroidism, dyslipidemia, and depression. She was diagnosed with stage IIa triple negative (estrogen receptor, progesterone receptor, and HER2/neu) breast cancer and had 10 Gy boost IORT followed by 37 Gy EBRT with adjuvant docetaxel/cyclophosphamide. She was not on steroids peri-procedure. Eight months after IORT and six months after EBRT, the patient complained of dyspnea and non-productive cough. Other etiologies were excluded and a CT of the chest showed patchy parenchymal densities on the irradiated side. She was treated with steroids but was still symptomatic a month later when she left the center.

There were no cases of radiation-induced COP and no deaths in 12 months. Further evaluation of the signs and symptoms mentioned previously did not yield any additional diagnoses of RP or COP.



**Figure 1:** Summary of IORT cases. IORT=Intraoperative radiotherapy; EBRT=external beam radiotherapy.

## Conclusion

In a single center retrospective cohort, IORT alone was not associated with pulmonary complications like RP and COP. Many patients (16.7%) had incomplete follow up, which could be attributed to transfer-of-care from this referral center or a patient's perceived treatment completion after initial therapy for an early stage breast

cancer. But they had no complications after an average 2.5 month follow-up. No patients receiving only IORT developed pulmonary complications. And there was only one case of radiation pneumonitis in this cohort, which was after boost IORT with EBRT. Of these, the EBRT is already well known to cause these complications. Thus IORT can continue to be used for early stage breast cancer in breast conserving surgery without worry of pulmonary complication. For

patients at high risk for pulmonary complication and high risk for breast cancer recurrence, further investigation should contrast the benefits of EBRT versus IORT alone.

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