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Integration of modern imaging into the multidisciplinary setting: The radiation oncology perspective

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A multidisciplinary approach to cancer diagnosis and treatment is vital to optimize care for the cancer patient. Multidisciplinary cancer management requires coordination among many different specialities involved in cancer care of an individual patient. Participants in this care include physicians from diverse oncology specialties, including surgical oncology, medical oncology, radiation oncology, pathology, radiology, nuclear medicine, genetic counseling, and depending on the tumor type, may also include various others from internal medicine and palliative care. In addition to physicians, there are nurses, nurse practitioners, physician assistants, and oncological nurse specialists that are involved in care, including patient navigators, clinic and research coordinators, and data managers as well as patient advocates and social workers.

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Benefits in care are multifactorial, arising from improvements in communication between disciplines leading to more efficient work-ups and decision making, which translates into improved outcomes for patients. To appreciate this point, several investigators have demonstrated that cancer care in a multidisciplinary setting is an independent predictor of improved outcomes. For example, Birchall[1] et al reported on patients with head and neck cancer in England before and after a report by the Calman-Hine Expert Advisory Group on Cancer,[2] recommending that designated cancer units and multidisciplinary care be established. They observed that patients receiving treatment in such a setting had an improved 2-year survival. Similarly, Junor[3] et al showed, in patients with ovarian cancer, that the multidisciplinary setting was an independent predictor for improved 5-year survival (65% versus 81%) compared to treatment outside this setting. Patients with Hodgkin's disease who were treated in a Surveillance, Epidemiology and End Results Program region were found to have 1.5 times higher cancer mortality as compared to patients treated at a Centralized Cancer Center, independent of age or stage of disease, suggesting that the process and quality of care was improved at the Centralized Cancer Centers.[4] These benefits are so convincing that the Commission on Cancer and the American College of Surgeons both require multidisciplinary conferences for the accreditation of health centers delivering multidisciplinary cancer care.[5-8]

One of the major benefits of multidisciplinary care is information sharing between various physicians where literature that is unique to their specialties and perspectives can be discussed, improving clinical care overall. In addition, centralized review of the pertinent patient-specific information, covering medical history, family history, physical exam findings, imaging studies, pathology results, while all cancer care specialists are present in the same conference room, is invaluable to the management of cancer patients and helps with

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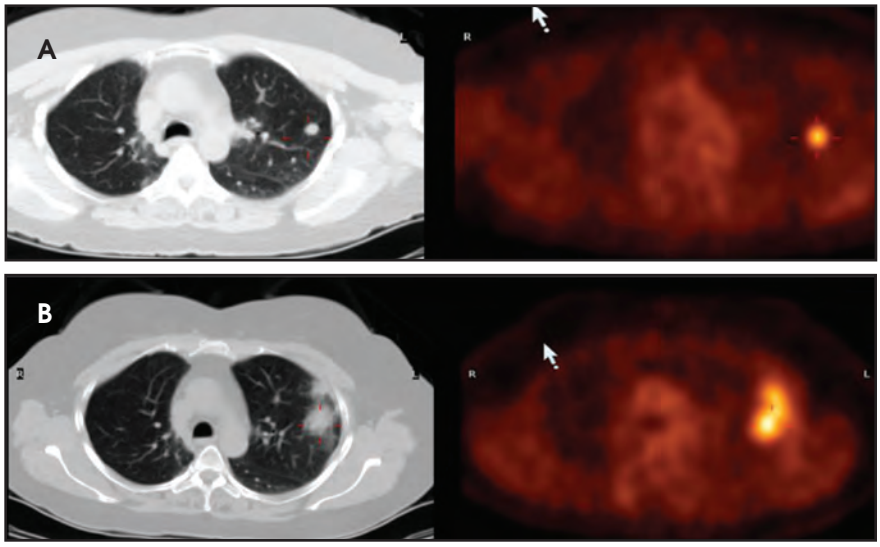

FIGURE 1. *CT and fused PET/CT images (A) pre-SBRT and (B) 3 months post-SBRT. Left upper-lobe lesion appears as patchy consolidation with some surrounding ground-glass opacities, which conformed to the intermediate dose of SBRT.*

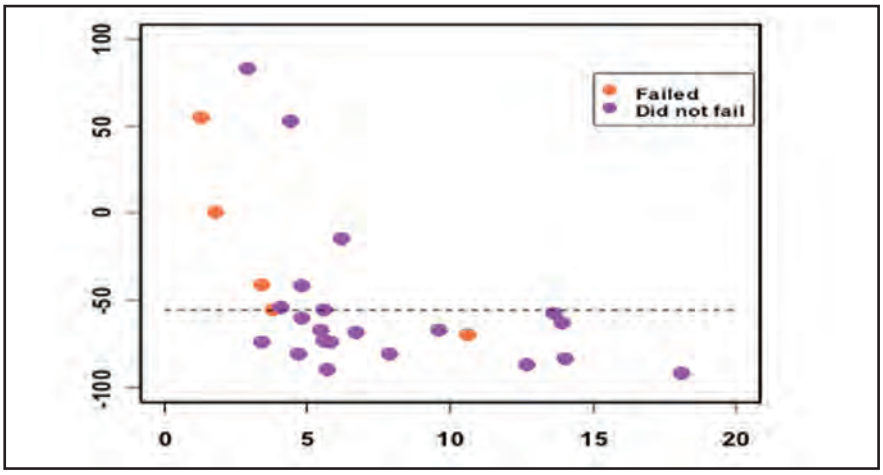

FIGURE 4. *This figure illustrates the response of therapy following SBRT (1 – (3-month post SBRT SUV max /pre SBRT SUV max)) on the y axis compared to the pre-SBRT max SUV. A drop of the 3-month-post-SBRT PET of 55% is the most important predictor of local control.*

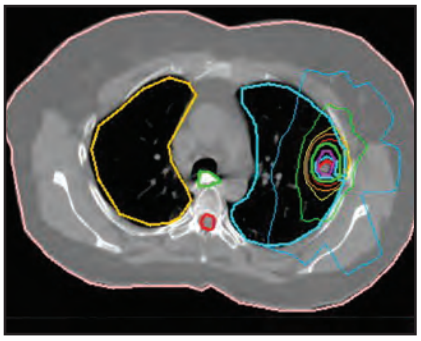

FIGURE 2. *This patient was treated with 5 nonopposing coplanar beams with isodose lines representing 20%, 50%, 90%, 100%, and 105% of the prescription dose.*

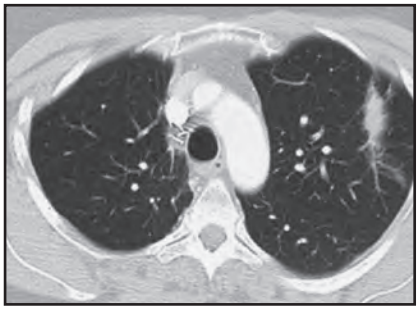

FIGURE 3. *Starting 9 months after radiotherapy, the patchy radiation changes seen 3 months following SBRT became more opaque and stretched in the direction of the dose fall-off as seen in Figure 2 and have remained stable for 5 years following SBRT (radiation fibrosis).*

immediate formulation of the recommendations for further management. Data suggest that multidisciplinary clinics are not just valuable for the participating physicians but also for their medical students, residents, and fellows who learn the value of a collaborative approach to management of complicated cases. The following cases illustrate how a multidisciplinary approach improves care with an emphasis on the impact of diagnostic radiology on cancer care.[9]

Case 1: Lung cancer

Ten years ago, there was no published prospective literature on ablative doses of radiation therapy for lung cancer (see below). Therefore, 2 of the authors of the current manuscript, Drs. Feigenberg and Yu, developed and opened a phase I dose escalation study[10] testing this novel technique, which had previously been successful in the management of inoperable brain tumors. As part of this study, the use of fluoro-deoxyglucose (FDG) positron emission tomography (PET)/computed tomography (CT) was incorporated into the treatment paradigm for patients with curable disease, with the specific purpose to use PET as a potential early biomarker for treatment response similar to what others had published in the setting of locally advanced disease.[11] As is often the case in phase I studies, this patient's situation created a clinical dilemma.

The patient was a young woman with lung cancer. Her first follow-up CT scan following trimodality therapy showed a new spiculated mass that was biopsied and demonstrated a second primary nonsmall cell lung cancer. She had just recovered from a lobectomy and did not feel she could undergo

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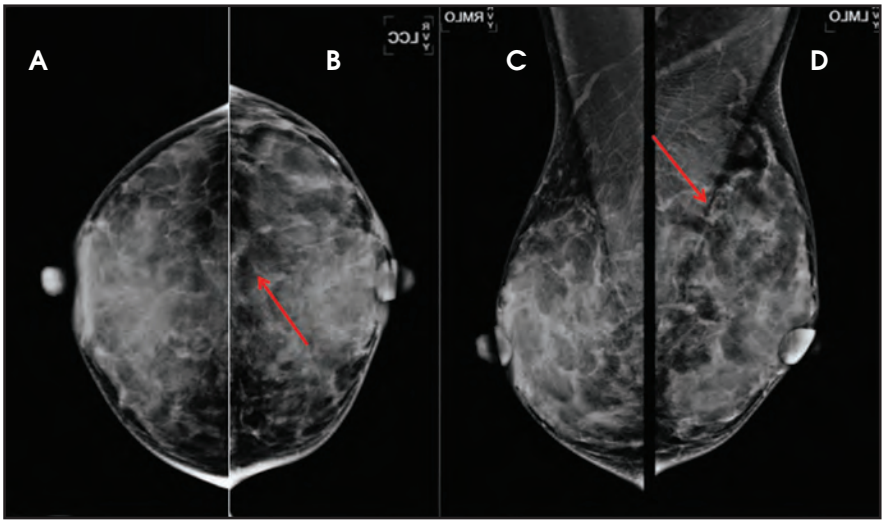

FIGURE 5. *40-year-old woman presenting for baseline screening mammogram. No family history of breast cancer or other risk factors for breast cancer. (A and B) Mammographic craniocaudal and (C and D) medio-lateral-oblique projections demonstrate extremely dense breasts with bilateral scattered and grouping calcifications with asymmetric distribution. The calcifications are more numerous in the left upper-outer quadrant and at 12 o'clock position in the left breast (B and D with arrow). No discrete mass or adenopathy is identified. BIRADS assessment category 0: additional magnification views of left breast recommended.*

further surgery. She was offered a novel treatment using stereotactic body radiotherapy (SBRT) on a phase I protocol as an alternative to a 7-week course of conventionally fractionated radiotherapy, which was the standard treatment at that time. She tolerated the SBRT treatment uneventfully, feeling well with no symptoms, and returned for her first post-therapy PET scan 3 months later as per the study protocol. At that time, images were not available in clinic, but the report was. The report read, "When compared to the last study dated 6/7/04, there has been a marked interval increase in the size of the previously noted left-upper lobe pulmonary nodule as well as increased intensity of FDG uptake in the area. The nodule has markedly increased in size and now extends out towards the pleural surface. The previous maximum standard uptake value (SUV) of 4.4 has increased to 6.7. This suggests that there has been no significant response to radiation therapy with progression of tumor growth."

As this was a medically operable patient, it was vital to review her images to determine further management. Her case was presented in conference, and it became glaringly obvious that the imaging findings were not as suspicious as the report indicated. Figure 1 demonstrates CT lung windows and the corresponding FDG PET prior to and 3 months' post-SBRT. Radiographic changes appeared as patchy consolidation with some surrounding ground-glass opacities as opposed to a solid mass-like lesion.

Dr. Feigenberg discussed the "new" treatment technique with his colleagues and demonstrated the differences in how the radiation dose could be delivered using many unique nonopposing coplanar and noncoplanar beams (Figure 2). This approach can cause a difference in the appearance of radiation pneumonitis that will more precisely conform to the tumor and will not have straight edges, typically seen using 2 opposing beams as was the standard approach.

Based on this factor, it was believed this abnormal PET finding was caused by an asymptomatic pneumonitis. It was recommended that surveillance be continued as opposed to any further intervention. Over time, the radiographically abnormal region became linear and denser, stretching in the direction of the radiation dose fall-off. This dense consolidation has remained stable for 5 years (Figure 2). This initial interaction led to several meaningful peer-reviewed presentations[10, 12, 13] and publications describing the importance of pre-SBRT PET values, post-SBRT PET values, and changes in PET values over the course of therapy (Figure 3). These findings are critical as this novel therapeutic radiation approach is currently challenging the paradigm of surgery[14] as standard of care for early stage lung cancer. This was the first data to illuminate concern of false positive results caused by radiation pneumonitis as well as the predictive value of a drop of the maximum SUV of 50%, required to ensure long-term local control.

Patient case 2: Breast cancer

Our multidisciplinary (multiD) Breast Cancer (BC) conference is held weekly before the multidisciplinary clinic and includes participants from all specialties involved in management. All newly diagnosed BC cases are presented, and pathology and imaging findings are discussed initially followed by preliminary workup and treatment recommendations. Patients are then seen on the same day in the multidisciplinary clinic held immediately after the conference by the 3 primary cancer specialists—surgical oncology, medical oncology, and radiation oncology. The recommendations are then made same day; the benefit of seeing newly diagnosed BC patients on the same day of the multiD conference is that the team can rapidly implement recommendations for further work-up if deemed necessary. In addition, the group can still consider the case or review the medical history and clinical findings given mutual accessibility at the same location.

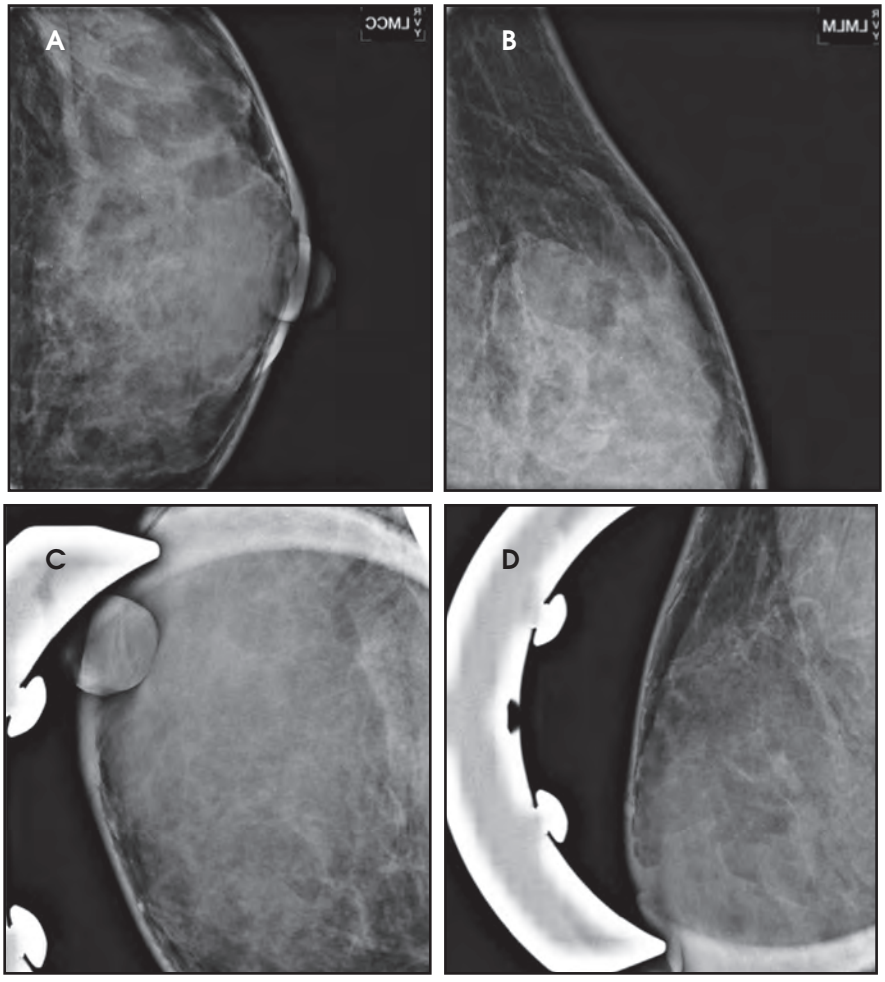

FIGURE 6. *Diagnostic mammogram: (A) Global magnification cranio-caudal and (B) latero-medial views of the upper outer left breast show multiple clusters of coarse heterogeneous, punctate, and amorphous calcifications. (C) Global magnification cranio-caudal and (D) latero-medial views of the right breast demonstrate diffuse scattered and grouped coarse, punctate and amorphous calcifications with no evidence of suspicious calcifications. BIRADS assessment Category 4: Suspicious finding. Stereotactic guided biopsy of the left breast recommended. Six-month follow-up of right breast calcifications recommended.*

The additional benefit to the patients is that they are seen by the 3 primary cancer specialists on one day and do not have to make several trips to be re-evaluated. Often patients are not aware that the management of BC may require treatments after surgery with radiation to the breast, hormonal therapy, and/or chemotherapy. These basic concepts of management of early-stage BC can also be introduced to the patients during their first visit to the multiD clinic.

The following case demonstrates many interactions between disciplines that are vital to patient care. A 40-year-old woman, with no known risk factors for breast cancer, presented for a baseline mammogram. This mammogram showed dense breasts with bilateral scattered and grouped calcifications with an asymmetric distribution, more numerous in the upper outer quadrant (Figure 5). The test was interpreted as incomplete, requiring additional evaluation with dedicated magnification views. When the patient returned for the additional diagnostic work-up, the morphology of the left breast calcifications was found to be suspicious, while the right breast calcifications were categorized as probably benign (Figure 6). Of note was that the breast thickness under mammographic compression was only 2.5 cm, usually a limiting factor to performing a needle biopsy under stereotactic guidance. The radiologist informed the patient of the results and need for biopsy. The patient was referred to the multidisciplinary breast clinic for further evaluation and discussion of treatment options.

Her case was presented to the multidisciplinary panel (breast imaging, breast surgery, medical oncology, radiation oncology, and breast pathology). Based on the imaging findings, the options of stereotactic-guided core and excisional biopsy were discussed. The patient elected to undergo a stereotactic-guided approach with the pathology demonstrating extensive atypical ductal hyperplasia. The case was discussed again in the multidisciplinary conference. Due to the presence of extremely dense breast tissue,[15, 16] an independent risk factor for breast cancer on mammogram, the patient's young age, and the newly diagnosed high-risk lesion, a breast MRI with gadolinium was recommended.

MRI demonstrated a 1-cm highly suspicious spiculated mass at the 12 o'clock position of the left breast and markedly asymmetric background parenchymal enhancement of the left breast compared to the right. Additionally, a nonspecific 1-cm left axillary node was also noted on MRI (Figure 7). The breast MRI was interpreted as suspicious. An ultrasound of the breast and the axilla confirmed the presence of 2 breast tissue abnormalities at 12 o'clock, believed to be highly suspicious for malignancy (Figure 8). The axillary node had a nonspecific appearance on ultrasound. The patient underwent biopsy of both masses and an ultrasound-guided fine-needle aspiration of the left axillary node. The larger 9-mm mass was an invasive ductal carcinoma, the smaller 8-mm mass was

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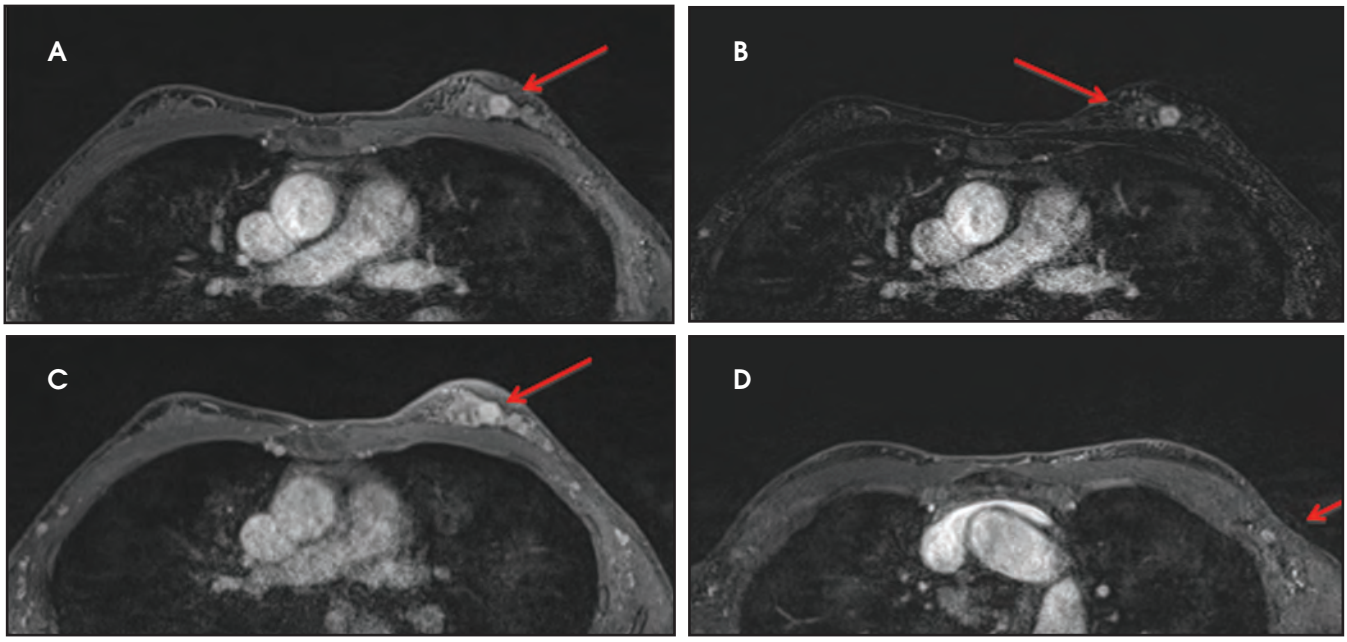

FIGURE 7. *Bilateral breast MRI: Preoperative breast MRI is requested by the surgeon as the patient is high risk due to extremely dense breasts and atypical ductal hyperplasia on core needle biopsy. (A) Axial fat-suppressed T1W and (B) corresponding subtracted image of the dynamic series is shown at first time point obtained 30 sec after injection of gadolinium based contrast. (C) High resolution axial T1W fat-suppressed image of the same image is shown 180 sec after injection of contrast. (D) Axial T1W fat-suppressed image of the axillary region is shown at the first time point. The background parenchymal enhancement is markedly asymmetric, being minimal on the right and moderate on the left (B with arrow). A highly suspicious 1-cm spiculated enhancing mass is noted at 12 o'clock position in the left breast (A with arrow) with no associated enhancement of the pectoral muscle or chest wall to suggest invasion. Correlation with mammogram (Figures 5A and 5B) demonstrates that this mass is in the vicinity of a cluster of suspicious calcifications noted on mammography. The mass demonstrates initial rapid enhancement and subsequent plateau enhancement (A and C). One left axillary lymph node demonstrates a mildly thickened cortex (D with arrow). No abnormal enhancement of the right breast or additional focal abnormal enhancement of the left breast or right axillary or internal mammary chain adenopathy is noted. BIRADS Assessment Category 5: Highly suspicious for malignancy. Recommendation: Left breast and axillary ultrasound and imaging-guided biopsy of the highly suspicious left breast mass.*

ductal carcinoma in situ, and the lymph node was positive for metastasis.

The patient was brought back to the multidisciplinary conference for a third time, where it was determined that the patient was not a good candidate for breast conservation due to the small size of her breast and a challenge for follow up due to diffuse calcifications and multifocal disease. Further discussion of the literature ensued regarding the possible need for radiotherapy and the role of a lymph node dissection.[17, 18] Delayed breast reconstruction[19, 20] was recommended to decrease the risks of loss of the implant due to encapsulation as compared to patients who undergo immediate reconstruction. Lastly, the role of axillary dissection was discussed. The recently conducted MRI evaluated the role of axillary dissection following positive sentinel lymph node biopsy[17]. The data were convincing that outcomes are not compromised by withholding dissection, although patients received radiotherapy to the whole breast, which indirectly also treats the majority of the axilla. [21, 22] In this case, since the patient was not going to receive radiotherapy following her mastectomy, an axillary dissection was recommended.

Patient case 3: Hepatocellular carcinoma

This case illustrates another example of how multiple disciplines were able to work together to convert an "incurable patient" to a "potentially curable patient." Orthotopic liver transplant (OLT)[23] is the only realistic curative treatment for patients with chronic hepatitis who are found to have hepatocellular carcinoma (HCC).

In May 2010, a 56-year-old man was diagnosed with HCC in the setting of chronic hepatitis C infection. At an outside institution, the patient was thought to have a solitary 4-cm ill-defined posterior lesion in the left lobe of the liver amenable to OLT. His alpha fetoprotein (AFP) level at presentation was 1500 ng/ml. While a transplant evaluation was being pursued, chemoembolization was performed twice in order to downstage the patient, producing a drop in AFP level to117 ng/ml, but the level rose to 566 ng/ml within 3 weeks. After transfer to the authors' institution, MRI with contrast demonstrated a cirrhotic liver with

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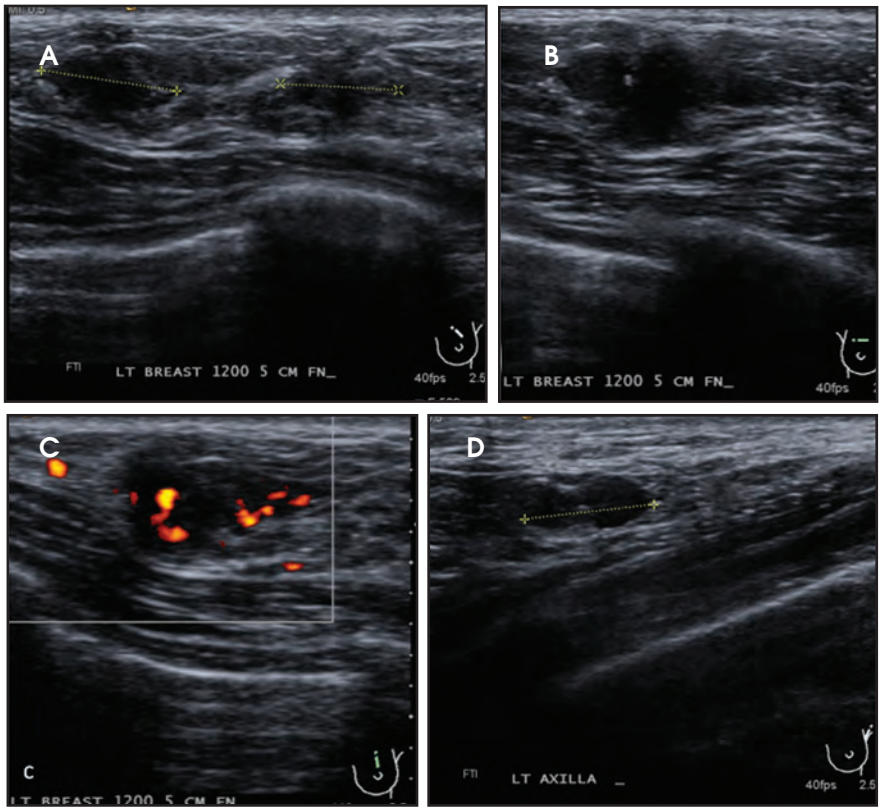

FIGURE 8. *Left breast and left axillary ultrasound. (A) Two contiguous similarly hypoechoic irregular solid masses are noted at 12 o'clock (calipers). Each mass is subcentimeter, measuring 9mm and 8mm. (B) The dominant 9-mm mass corresponds to the highly suspicious mass seen on MRI (Figures 7A - C) and (C) demonstrates significant vascularity. The second similar smaller 8-mm mass corresponds to confluent enhancing foci on MRI. (D) Ultrasound of the left axilla demonstrates the 9-mm lymph node with thickened cortex noted on MRI and is categorized as suspicious. Overall, the BIRADS assessment is confirmed as category 5, highly suspicious for malignancy. Recommendation: Ultrasound-guided core-needle biopsy of both masses and ultrasound-guided fine-needle aspiration of the left axillary lymph node.*

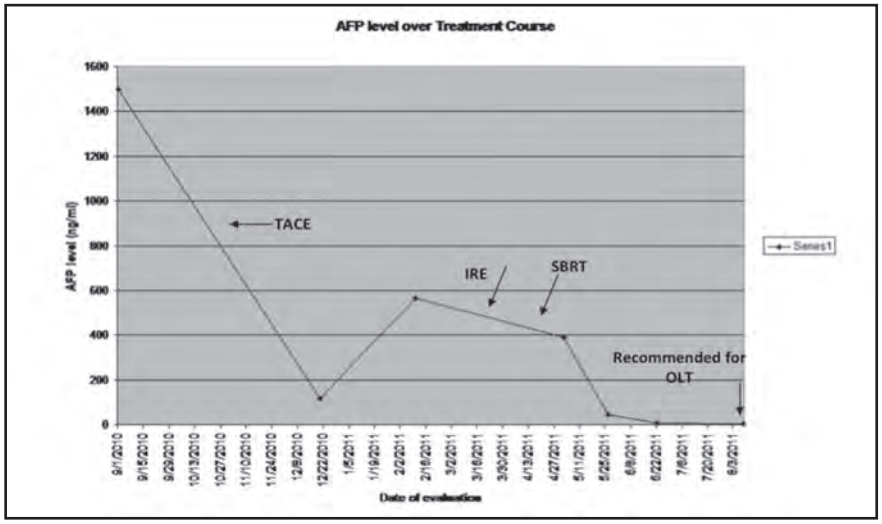

FIGURE 10. *AFP level with critical treatment milestones.*

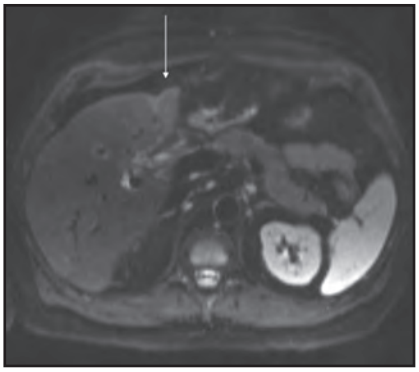

FIGURE 9. *First post-IRE/SBRT MRI scan demonstrating left lobe atrophy (arrow).*

multifocal enhancing masses in hepatic segment IV consistent with persistent HCC. In addition, there was a suggestion of tumor invasion and thrombosis of the left portal vein excluding him from OLT. Due to his overall excellent performance status, his case was discussed at the multidisciplinary hepatobiliary tumor board and "spirited" discussions among the present medical, surgical, radiation oncologists, interventional and diagnostic radiologists ensued. Due to the size of the lesion, all single-modality therapies were thought to have poor local control potential so a combination therapy was considered as the best method to potentially eradicate the large residual tumor. This approach entailed targeting the tumor through a combination of irreversible electroporation (IRE)[22, 23] performed by interventional radiology, followed by SBRT[24, 25] performed by radiation oncology. The rationale for this approach was to get a direct tumoricidal effect through IRE[24, 25] initially, and to then cover the core and periphery (including the portal vein component) of the ablated region with high-dose SBRT.[26, 27]

The patient underwent CT-guided IRE on 3/22/2011 and tolerated his treatment well. Subsequently, the patient underwent 4-dimensional simulation (to account for tumor movement with the respiratory cycle) and a 5-fraction treatment of 6 Gy each was delivered to a large portion of the left lobe.

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The total dose of 30 Gy was administered over a 9-day period ending on 4/20/11, also tolerated well by the patient. A repeat MRI on 5/16/2011 demonstrated interval atrophy of the left lobe (Figure 9) with no residual enhancement and consistent with tumor regression/resolution. AFP levels (measured in ng/ml) continued to drop to 390.8 on 5/2/11, 44.7 on 5/26/11, 6.6 on 6/22/11, and 4.8 on 8/8/11 (Figure 10).

Restaging PET and bone scans along with subsequent MRI studies continued to demonstrate no further abnormal activity compatible with disease recurrence. The patient was again presented to the multidisciplinary hepatobiliary tumor board in September. Given the dramatic decline in AFP levels without evidence of recurrent or metastatic HCC, the patient was reconsidered for OLT and was subsequently placed back on the active transplant list.

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