Personalized Medicine in Action: The Case of Intensity Modulated Radiation Therapy

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PRELIMINARY

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Abstract: Breast cancer patients typically receive either conventional beam radiation or intensity modulated radiation therapy (IMRT) following surgery. Medicare spending is $8,000 higher for patients who receive IMRT, but there is little evidence that IMRT is superior to conventional beam radiotherapy. Using SEER-Medicare data, we show that patients treated in freestanding radiation therapy centers, most of which are physician-owned, are substantially more likely to receive IMRT. Use of a readily-observable marker of patients' ability to benefit from IMRT, tumor laterality, has a strong impact on its use. However, incentives affect how physicians incorporate the marker into treatment decisions: patients treated in freestanding centers are more likely to receive IMRT regardless of whether their tumor is in the left or right breast. These results highlight the challenge of maximizing the benefit of tests that imperfectly predict patients' ability to benefit from a treatment in an environment where physicians' compensation is tied to the volume of treatments they provide.

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Introduction

Proponents of personalized medicine frequently claim that personalized medicine tests will reduce health care spending (for example, PhRMA 2015). The argument goes like this: If a test identifies a group of patients unlikely to benefit from a costly treatment, then physicians can save money by using a different, less costly treatment in that group. Besides assuming all patients would receive the costly treatment in the absence of the test, the claim assumes that personalized medicine tests clearly identify patients who can and cannot benefit from treatment and that providers, many of whom are paid on a fee-for-service basis, will use the information even if it is not in their financial interest to do so. In reality, many personalized medicine tests identify patients unlikely to benefit only in a probabilistic sense. Far from simplifying treatment decisions, most personalized medicine tests introduce yet another prognostic factor for physicians to consider (Hunter et al. 2016). Physicians who face strong financial incentives to provide a treatment may conveniently discount a test result indicating a patient is less likely to benefit from the treatment.

In this paper we use the case of intensity modulated radiation therapy (IMRT) in women with breast cancer to illustrate this point. IMRT is a form of radiotherapy. It costs about $8,000 more than conventional radiotherapy. We can distinguish between two groups of providers based on their incentives to provide IMRT: hospital-based and freestanding radiotherapy clinics. Likewise, we can divide patients into two groups based on their ability to benefit from IMRT. We present data on how these factors interact. We find that fewer women in the low benefit group receive IMRT, but the proportion of women in the low benefit group who receive IMRT in freestanding clinics is actually higher than the proportion of women in the high benefit group who receive IMRT in hospital-based clinics. Our results suggest that the realized efficiency gains from the introduction of personalized medicine tests will depend on the financial incentives facing providers.

In related work, Dinan et al. (2015) report that receipt of the 21-gene recurrence score assay, a test which predicts breast cancer patients' ability to benefit from chemotherapy, was not associated with lower rates of use of chemotherapy among breast cancer patients. However, only 10% of the patients in the sample received the test. Cross sectional comparisons may be biased by other patient characteristics related to the ability to benefit from chemotherapy and the receipt of the test. In our case, tumor laterality is readily observable to all physicians, and so estimates of the impact of the information are unbiased by unobserved factors related to providers' decisions to obtain it.

Clinical background

Women with early stage breast cancer are typically offered the choice between mastectomy and breast conserving surgery (also known as lumpectomy). Following breast conserving surgery, where surgeons remove visible masses of tumor cells, most patients undergo radiation therapy to kill any remaining tumor cells. Therapy is delivered on an outpatient basis. Conventional external beam radiation therapy can damage healthy cells near the target site, leading radiation oncologists to seek methods of delivering radiation that spare the tissue surrounding the target. Unlike conventional beam radiation, IMRT uses sophisticated treatment planning software to ensure that the target area receives a consistent, uniform dose while minimizing the delivery of radiation to nearby tissue. IMRT is commonly used as a primary

therapy for head and neck cancer and prostate cancer. While IMRT reduces the delivery of high dose radiation to critical anatomic structures, it also "scatters" more low dose radiation compared to conventional radiotherapy (Shubert et al. 2011; Zhang et al. 2011). However, the net effect is thought to favor IMRT.

Several randomized trials have compared IMRT to conventional radiotherapy in breast cancer patients benefits (Mukesh et al. 2013; Pignol et al. 2008). They found that patients treated with IMRT were less likely to experience cosmetic side effects and self-limiting skin peeling and irritation but had similar quality of life, tumor recurrence rates, and survival rates. Based on the lack of evidence that IMRT is associated with clinically significant benefits, the American Society for Radiation Oncology (2013) recommends against routine use of IMRT in breast cancer patients following breast conserving surgery. Medicare spending is $6,000 to $8,000 higher for breast cancer patient who receive IMRT compared to conventional radiotherapy (Roberts et al. 2013; Smith et al. 2011).

Radiotherapy risks damaging the heart. The risk is higher for women with tumors in the left breast. For this reason, the value of IMRT is higher for women with left-sided tumors. Some Medicare claims processors and Medicare Advantage plans include the following language in their IMRT coverage policies, "Indications will include some left breast tumors due to risk to immediately adjacent cardiac and pericardial structures, though it would only rarely if ever be medically necessary for tumors of the right breast." Even for women with left-sided tumors, the value of IMRT is questionable for most patients. The use of relatively inexpensive techniques and technologies, like breath-holding or shields, can reduce the exposure of the heart to radiation.

Physicians' treatment setting

Cancer patients can receive radiotherapy at freestanding clinics, most of which are owned by the radiation oncologists who practice there, or hospital-based clinics. Some hospitals employ radiation oncologists, and in recent years many hospitals have purchased radiation oncology groups. However, during the period covered by our study, most hospital clinics were staffed by radiation oncologists in independent groups. In some cases hospitals and independent radiation oncology groups co-manage a radiation oncology clinic.

Delivery of IMRT is a complex, multi-step process that includes treatment planning, physician management, imaging procedures, and treatment delivery. Clinics bill separate Current Procedural Terminology (CPT) codes for each step. Some are billed only once, others are billed on a recurring basis. According to online patient education materials, patients typically undergo 25 to 40 sessions. Radiology clinics bill a code for treatment delivery for each session. There is no professional fee associated with the code, but the facility fee for treatment delivery in a freestanding clinic is approximately $500, accounting for a substantial share of the total revenues associated with IMRT. Medicare sets facility fees to coverage average costs. The difference between average and marginal costs may be especially large for capital-intensive services like IMRT. The fee for treatment delivery of conventional beam radiation therapy is around $100.

Radiation oncologists in independent practices receive a salary and possibly a bonus tied to the professional fees they generate. Radiation oncologists who are owners also receive a share of the group's profits. Radiology groups whose physicians staff hospital clinics bill for the professional fees only. Groups that co-manage a hospital clinic may also receive a management fee that is set independently of the volume of care the physicians provide. Freestanding radiation clinics and hospitals that employ radiation oncologists bill for both professional and facility fees. They cannot pay facility fees directly to physicians based on the volume of care they provide (it

would violate Medicare anti-kickback regulations). Instead, facility fees augment the profits that are distributed to owners. For this reason, physicians in freestanding clinics may face extra incentives to provide IMRT instead of conventional radiotherapy compared to physicians practicing in other types of settings.

Studies on how physician incentives affect the use of IMRT have mostly focused on the treatment of prostate cancer. A 2010 *Wall St. Journal* article (Carreyrou and Tamman 2010) described how companies like Urorad Healthcare help urology practices set-up their own IMRT centers. According to the article, Integrated Medical Professionals, a large urology group in New York, owns 11 linear accelerators. Half the patients treated by the practice undergo IMRT. Three studies (Bekelman et al. 2013; General Accounting Office 2013; Mitchell 2013) have found that the acquisition of IMRT equipment by a urology group increases the share of prostate cancer patients receiving IMRT versus prostatectomy or other treatments by about 15% percentage points. Despite using different patient samples and methods for identifying self-referring practices, the studies were remarkably consistent in their findings. Studies examining the determinants of radiotherapy treatment patterns among breast cancer patients have found that patients treated in freestanding clinics are substantially more likely to receive IMRT (Roberts et al. 2013; Smith et al. 2011). It is unclear to what degree these differences are attributable to unobserved patient characteristics.

In other clinical settings, a number of studies have shown that when physicians assume ownership stakes in facilities or equipment, their procedure volume rises (Baker 2010; Barro et al. 2006; Hollenbeck et al. 2010; Hollingsworth et al. 2010a; 2010b; 2011; Iizuka 2007; 2012; Mitchell 1992; 2005; 2008; 2010l, Nallamothu et al. 2007; Shreibati and Baker 2012). These results strongly suggest that the incentives inherent in physician ownership affect physicians' treatment decisions, though there are alternative explanations. Physicians' responses could reflect the convenience of having equipment on-site, or physicians may purchase ownership stakes in anticipation of planned changes in practice patterns. For example, orthopedic surgeons who want to specialize in outpatient surgeries may buy ownership stakes in ambulatory surgery centers. Physicians who believe that a treatment is effective may be more likely to take an ownership stake in the facility or equipment necessary to deliver it.

The setting for our study differs in some respects from that of previous studies of physician ownership. Most previous studies examine changes or differences in the volume of a particular procedure. In our case, all patients receive treatment, either IMRT or another form of radiotherapy. This feature facilitates identification because we observe patients who do and do not receive the treatment in question. Also, by 2007, the midpoint of our data, nearly all radiation therapy clinics had the capability to perform IMRT. Variation in use cannot be explained in terms of differences in convenience or availability. Radiation oncologists may specialize in the treatment of specific tumor types, but they do not specialize in the delivery of IMRT. Comparisons between freestanding and hospital-based clinics are not biased by differences in the degree of specialization in particular types of radiotherapy.

Data

We estimate the determinants of the receipt of IMRT using SEER-Medicare data. SEER-Medicare includes tumor registry records from regional SEER tumor registries linked with Medicare claims for Medicare-eligible beneficiaries. The SEER registries capture 100% samples of cancer patients from California, Georgia, Iowa, Hawaii, Utah, Kentucky, Louisiana, New

Mexico, Connecticut, Detroit, and Seattle. From SEER Medicare we selected a sample of women who were diagnosed with early or regional stage breast cancer between 2000 and 2011 (the latest year available), were 66 years of age or older, were continuously enrolled in fee-for-service Medicare in the 24 month window centered on the diagnosis date, underwent breast conserving surgery, and received post-operative radiotherapy. Details are presented in Table 1. For many analyses we limit the sample to women diagnosed in or after 2007 to measure treatment patterns following the initial diffusion of IMRT.

Table 1: Sample construction

Included	Excluded	Criteria
113,891		Surgery for breast cancer between 2000-2011
72,349	41,542	Had a claim for radiotherapy
67,417	4,932	Radiotherapy within 365 days of surgery
61,030	6,387	Received breast conserving surgery
50,175	10,855	Age >=66 and continuously enrolled in Medicare
50,061	114	Stage at diagnosis known
49,670	391	Early or regional stage (non-metastatic)
48,137	1,533	Received surgery within 90 days of diagnosis
20,205	27,932	Treated in or after 2007[a]

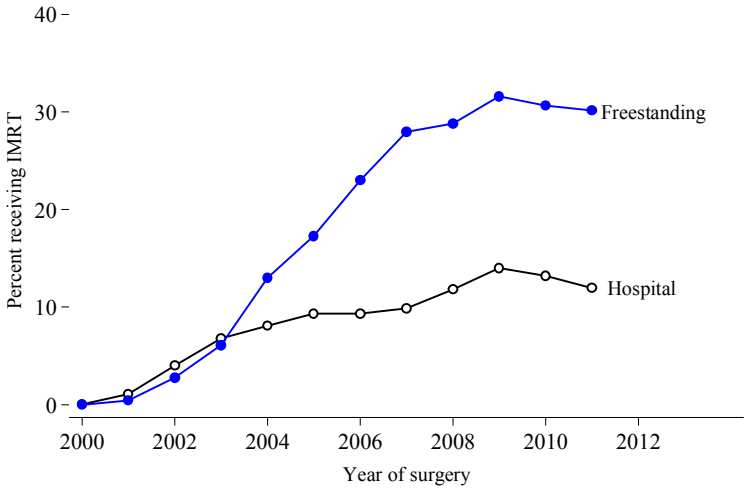
[a]Used in selected analyses

The primary outcome is the receipt of IMRT versus another form of radiation therapy. We categorize provider type as free-standing versus hospital based on whether the initial radiotherapy claim appeared in the National Claims History file or the outpatient file. We used a similar approach to categorize the type of provider where the patient received surgery. We further categorized hospital radiotherapy clinics based on the type of hospital using the hospital characteristics file included with the SEER-Medicare data.

Trends in treatment patterns

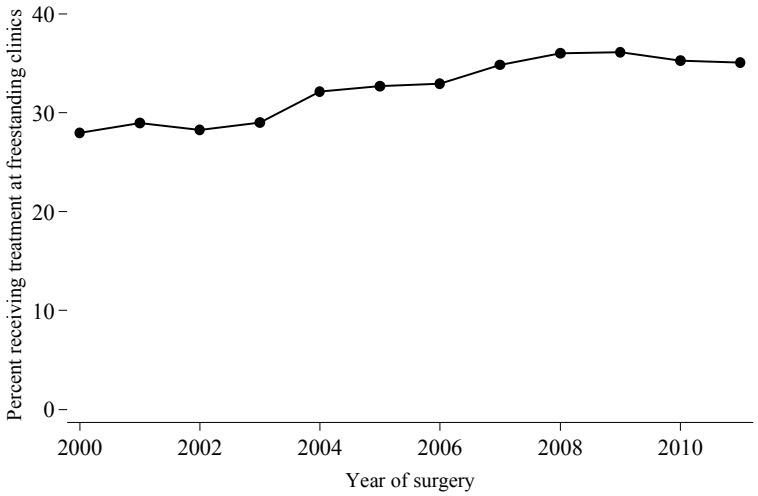
Figure 1 shows the proportion of patients receiving IMRT by provider type. Initially, patients in hospital-based clinics were slightly more likely to receive IMRT. Clinics had to spend over $2,000,000 to acquire the equipment to provide IMRT, and hospitals may have an advantage over freestanding clinics in financing investments in costly capital equipment. By 2007 28% patients treated in freestanding clinics received IMRT compared with only 12% percent in hospital clinics. We do not have data on the date when clinics acquired the capability to perform IMRT. IMRT quickly became the standard of care for prostate and head and neck tumors. Based on conversations with radiation oncologists, we believe that nearly all clinics had the capability to delivery IMRT by 2008 if not earlier.

Figure 1: Patients receiving IMRT by provider type



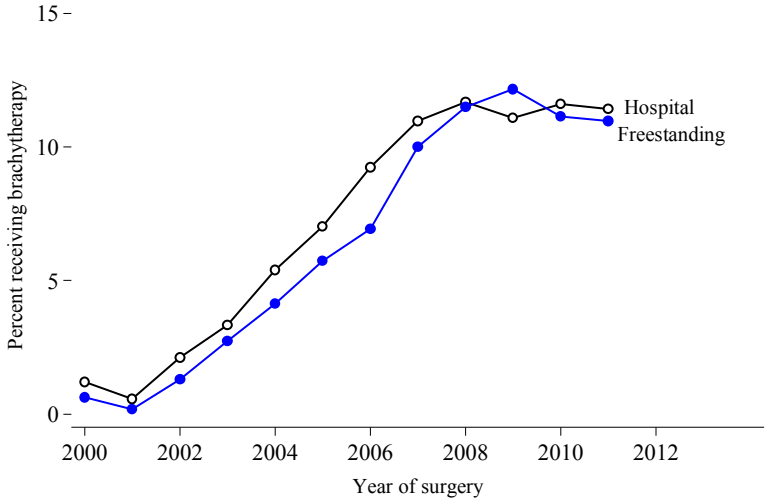
The difference in practice patterns between freestanding and hospital-based facilities is striking, but we cannot rule out the possibility that the difference is due to differences in patients' clinical characteristics or preferences for advanced technology. Below we present a number of additional analyses to show that there is a causal relationship between provider type and the receipt of IMRT. Figure 2 shows trends in the proportion of patients receiving radiotherapy at freestanding clinics. The share has gone up slightly over time.

Figure 2: The share of patients receiving radiotherapy at freestanding clinics



Brachytherapy is an alternative to conventional beam radiotherapy and IMRT. As shown in Figure 4, equal shares of patients treated in freestanding and hospital-based clinics receive brachytherapy. Brachytherapy requires the implantation of a catheter to deliver the radioactive seeds. In breast cancer patients the implantation typically occurs during surgery, which proceeds radiotherapy, and so radiation oncologists have less influence over the use of brachytherapy.

Figure 3: Patients receiving brachytherapy by provider type



Regression-adjusted differences

We use logistic regression to estimate differences in the receipt of IMRT between freestanding and hospital-based clinics among patients treated in or after 2007, adjusted for observable patient characteristics. Table 2 presents sample means. Most of the markers of disease severity – tumor size, whether cancer is detectable in the lymph nodes near the breast, and whether the stage at diagnosis is local or regional – are similar between patients treated in hospital-based and freestanding clinics. Women treated in hospital-based clinics are more likely to have estrogen-receptor-positive tumors. Women with estrogen-receptor-positive tumor have a better prognosis. Most of the other variables are self-explanatory. The variable "restrictive coverage" indicates whether the patient lived one of the SEER regions where the Medicare carrier had a policy that limited coverage or IMRT (California, Hawaii, Iowa, New Jersey, Washington, Utah) and allowed providers to bill for IMRT only if they provided "inverse planned" IMRT rather than "forward planned" IMRT. Under inverse-planned IMRT, the radiation oncologist specifies target radiation doses for various tissues and a computer program identifies a treatment plan by solving the constrained optimization problem. Under forward-planned IMRT, the radiation oncologists provides an initial plan and then uses optimization and a trial-and-error process to improve upon it.

Table 2: Patient characteristics

	All patients	Radiotherapy clinic type		P-value
		Freestanding	Hospital	
		N (%)		
Freestanding clinic	7,161 (35.4)	7,161 (100.0)	0 (0.0)	
Tumor size >3 cm	4,479 (22.2)	1,597 (22.3)	2,882 (22.1)	0.735
Positive lymph nodes	3,189 (15.8)	1,161 (16.2)	2,028 (15.5)	0.215
Left-side tumor	10,264 (50.8)	3,609 (50.4)	6,655 (51.0)	0.398
Local stage	16,764 (83.0)	5,903 (82.4)	10,861 (83.3)	0.132
ER positive	17,238 (85.3)	5,943 (83.0)	11,295 (86.6)	<0.001
Age				0.150
65-74	11,392 (56.4)	4,103 (57.3)	7,289 (55.9)	
75-84	7,513 (37.2)	2,609 (36.4)	4,904 (37.6)	
85+	1,300 (6.4)	449 (6.3)	851 (6.5)	
Race				0.067
White	17,874 (88.5)	6,356 (88.8)	11,518 (88.3)	
Black	1,255 (6.2)	404 (5.6)	851 (6.5)	
Asian	405 (2.0)	144 (2.0)	261 (2.0)	
Hispanic	204 (1.0)	82 (1.1)	122 (0.9)	
Other	467 (2.3)	175 (2.4)	292 (2.2)	
Region				<0.001
Pacific	7,995 (39.6)	3,245 (45.3)	4,750 (36.4)	
East	8,729 (43.2)	2,815 (39.3)	5,914 (45.3)	
North	2,252 (11.1)	611 (8.5)	1,641 (12.6)	
Other	1,229 (6.1)	490 (6.8)	739 (5.7)	
Medicaid coverage	1,777 (8.8)	685 (9.6)	1,092 (8.4)	
Rural/less urban	2,431 (12.0)	950 (13.3)	1,481 (11.4)	
Year				0.689
2007	3,851 (19.1)	1,349 (18.8)	2,502 (19.2)	
2008	3,869 (19.1)	1,400 (19.6)	2,469 (18.9)	
2009	3,954 (19.6)	1,403 (19.6)	2,551 (19.6)	
2010	4,151 (20.5)	1,479 (20.7)	2,672 (20.5)	
2011	4,115 (20.4)	1,446 (20.2)	2,669 (20.5)	
N	20,205	7,161	13,044	

ER positive: estrogen receptor positive tumor.

The first column of Table 3 displays marginal effects from a probit regression. The dependent variable equals 1 if the patient received IMRT and 0 if the patient received another form of radiotherapy. Standard errors are clustered at the clinic level. Controlling for patient characteristics, patients who received radiotherapy in freestanding clinics at 18 percentage points more likely to receive IMRT.

The proportion of patients receiving IMRT is 7 percentage points higher among patients with tumors in the left breast. Most of the other patient characteristics have only small, non-significant effects. Patients in SEER regions where the Medicare carrier has a restrictive coverage policy are less likely to receive IMRT.

Table 3: Marginal effect on the likelihood of receiving IMRT from probit regressions

	Probit			IV probit			IV probit, patients who received surgery in hospitals only		
	Marginal effect (95% CI)								
Freestanding clinic	0.18	(0.11, 0.25)	**	0.19	(0.07, 0.31)	**	0.21	(0.09, 0.33)	**
Left-side tumor	0.07	(0.05, 0.09)	**	0.07	(0.05, 0.09)	**	0.07	(0.05, 0.09)	**
Tumor size >3 cm	0.00	(-0.02, 0.01)		0.00	(-0.02, 0.01)		0.00	(-0.02, 0.01)	
Positive lymph nodes	0.00	(-0.05, 0.05)		0.00	(-0.05, 0.05)		-0.01	(-0.06, 0.04)	
Local stage	-0.01	(-0.06, 0.03)		-0.01	(-0.06, 0.03)		-0.02	(-0.07, 0.02)	
ER positive	0.00	(-0.02, 0.02)		0.00	(-0.01, 0.02)		0.01	(-0.01, 0.02)	
Age 75-84	0.01	(-0.00, 0.02)		0.01	(-0.00, 0.02)		0.01	(-0.00, 0.02)	
Age 85+	-0.02	(-0.04, 0.01)		-0.02	(-0.04, 0.01)		-0.02	(-0.05, 0.01)	
Black	0.03	(-0.01, 0.07)	+	0.03	(-0.01, 0.07)	+	0.02	(-0.02, 0.06)	
Asian	-0.03	(-0.08, 0.02)		-0.03	(-0.08, 0.02)		-0.01	(-0.07, 0.04)	
Hispanic	-0.03	(-0.11, 0.04)		-0.03	(-0.11, 0.04)		-0.02	(-0.11, 0.07)	
Other	-0.04	(-0.09, 0.01)		-0.04	(-0.09, 0.01)		-0.04	(-0.09, 0.02)	
Medicaid coverage	-0.03	(-0.06, -0.00)	*	-0.03	(-0.06, -0.00)	*	-0.04	(-0.07, -0.01)	**
Rural/less urban	-0.06	(-0.11, -0.01)	*	-0.06	(-0.11, -0.01)	*	-0.06	(-0.11, -0.01)	*
Restrictive coverage	-0.16	(-0.23, -0.09)	**	-0.16	(-0.23, -0.09)	**	-0.17	(-0.24, -0.09)	**
2008	0.02	(0.00, 0.05)	*	0.02	(0.00, 0.05)	*	0.02	(0.00, 0.05)	*
2009	0.04	(0.01, 0.07)	**	0.04	(0.01, 0.07)	**	0.03	(0.00, 0.07)	*
2010	0.03	(0.00, 0.06)	*	0.03	(0.00, 0.06)	*	0.02	(-0.01, 0.05)	
2011	0.02	-0.01 0.05		0.02	-0.01 0.05		0.02	-0.02 0.05	
N	20,205			20,205			16,455		

+p<0.10;*p<0.05;**p<0.01

We performed an instrumental variables analysis to confirm that differences in the receipt of IMRT are not biased by unobserved patient characteristics. We use the type of provider where patients received surgery as an instrument. Patients receive surgery in one of three types of providers 1) freestanding surgery centers, 2) hospitals with radiation oncology clinics, and 3) hospitals that do not have radiation oncology clinics. We hypothesized that patients who receive surgery in hospitals with radiation oncology clinics will be more likely to receive radiotherapy at a hospital-based clinic. The identifying assumption is that the patient characteristics that predict whether patents receive IMRT (conditional on observables) do not predict what the type of provider at which patients receive surgery. These characteristics could include clinical characteristics like the proximity of the tumor to healthy vital tissues that could be damaged by radiation exposure and personality traits like a preference for advanced technology.

Figure 4 shows the proportion of patients who receive post-operative radiotherapy by surgery provider type. Compared to patients who receive surgery in freestanding surgery centers and patients who receive surgery in hospitals that do not offer radiotherapy, patients who receive surgery in hospitals that do offer radiotherapy are about 5 and 3 percentage points more likely to receive post-operative radiotherapy. However, these differences are small in percentage terms given that 80% of women receive post-operative radiotherapy.

Table 4 shows patient characteristics by surgery provider type. Based on differences in tumor size, the number of positive lymph nodes, and stage, patients receiving surgery in freestanding centers appear to have worse prognoses. These characteristics do not necessarily predict patients' ability to benefit from IMRT. The most important observable characteristic for predicting patients' ability to benefit from IMRT is whether the tumor is in the left or right breast. The left breast is closer to the heart. Equal shares of patients in each type of surgery provide have left breast tumors, suggesting that unobserved clinical characteristics related to patients' ability to benefit from IMRT are equally distributed.

Figure 4: Proportion of patients undergoing post-operative radiotherapy by surgical provider type

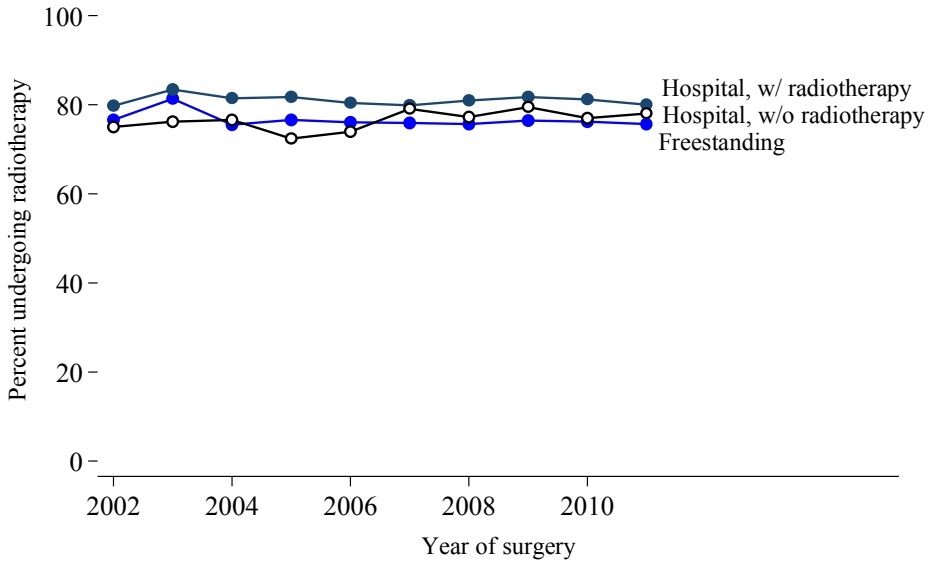


Table 4: Patient characteristics by surgery provider type

	Surgery provider type			
	Freestanding	Hospital without radiotherapy	Hospital with radiotherapy	P-value
	N (%)			
Tumor size >3 cm	950 (25.3)	1,138 (21.3)	2,391 (21.5)	<0.001
Positive lymph nodes	817 (21.8)	810 (15.2)	1,562 (14.0)	<0.001
Local stage	2,886 (77.0)	4,450 (83.4)	9,428 (84.8)	<0.001
ER positive	3,144 (83.8)	4,455 (83.5)	9,639 (86.7)	<0.001
Left-side tumor	1,895 (50.5)	2,701 (50.6)	5,668 (51.0)	0.870
N	3,750	5,333	11,122	

Table 5 shows the proportion of patients receiving radiotherapy in a freestanding clinic and IMRT across surgery provider types. Among patients receiving surgery in a freestanding surgery center, 38.1% receive radiotherapy in a freestanding clinic. Among patients receiving surgery in hospitals without a radiotherapy clinic, 70.2% received radiotherapy in a freestanding clinic compared to only 17.9% of patients who received surgery in a hospital with a radiotherapy clinic. Patients treated at freestanding radiotherapy centers are more likely to receive IMRT across all survey provider types. Overall, patients treated at hospitals without radiotherapy centers are more likely to receive IMRT, reflecting the fact that 70.2% receive radiotherapy in freestanding clinics. Somewhat surprisingly, the share of patients receiving IMRT does not differ substantially between patients treated in freestanding surgery centers and hospitals with radiotherapy clinics (16.5% and 16.1%).

Table 5: Receipt of IMRT among patients treated in or after 2007 by setting

			Surgery provider type					
Radiotherapy facility	All		Freestanding		Hospital without radiotherapy		Hospital with radiotherapy	
	Percent receiving IMRT, Number receiving IMRT/Total							
Freestanding clinic	35.4%	7,161/20,205	38.1%	1,429/3,750	70.2%	3,744/5,333	17.9%	1,988/11,122
IMRT by provider type								
Freestanding	29.9%	2,138/7,161	27.0%	386/1,429	30.1%	1,128/3,744	31.4%	624/1,988
Hospital	12.2%	1,589/13,044	10.0%	232/2,321	12.1%	193/1,589	12.7%	1,164/9,134
IMRT	18.4%	3,727/20,205	16.5%	618/3,750	24.8%	1,321/5,333	16.1%	1,788/11,122

The second set of regression results in Table 3 shows marginal effects from an IV probit model, fit in a single step using maximum likelihood, with standard errors clustered at the clinic

level. The instrument is a dichotomous variable equal to 1 if the patient received surgery at a hospital that offers radiation therapy. The coefficient on the instrument from a "first stage" linear probability model that assess the impact of the instrument and the other independent variables on the likelihood of receiving radiation therapy in a freestanding clinic is -0.38 (i.e., 38 percentage points) and is significant at the 1% level.

Results from the IV probit model are similar to those from the baseline model. The F-statistic associated with the instrument is 152. The exclusion restriction would be violated if patients with unobservable tumor characteristics related to their ability to benefit from IMRT were more or less likely to receive surgery in hospitals with radiotherapy clinics. There are some differences in observable characteristics between patients who received surgery in freestanding surgery centers and hospitals, though not in terms of the characteristic that is closely related to patient benefit: whether the tumor was in the left or right breast.

Among patients who received surgery at a hospital, observable tumor characteristics are similar between patients who received surgery at a hospital that offers radiotherapy and patients who received radiotherapy at a hospital that does not offer radiotherapy. The third set of regression results are from an IV probit model estimated on the subsample of patients who received surgery at a hospital. Marginal effects are similar to those from the other models. The exclusion restriction would also be violated if patients who have preferences for advanced medical technology are more likely to receive surgery at freestanding surgery centers or hospitals that do not have a radiotherapy clinic. Perhaps women who have a strong preference for IMRT go to freestanding centers if their requests are refused at hospital-based centers. But this begs the question: Why, apart from financial incentives, would physicians at freestanding center be more likely to indulge patient requests?

Practice setting and personalized medicine

Based on the models presented in Table 3, use of IMRT is 7 percentage points higher among women with left-sided tumors. There is a difference in treatment patterns based on tumor laterality, but not as much as one might expect based on coverage policies that state that IMRT "…would only rarely if ever be medically necessary for tumors of the right breast." The incentives facing providers may lead them to overtreat women with right-side tumors.

Table 6 shows the proportion of patients receiving IMRT by tumor laterality and practice setting. We present results separately for patients in SEER regions where carriers have no IMRT coverage policies and areas where they have restrictive policies, which emphasize the relative benefits of using IMRT for left versus right-breast tumors and do not pay higher rates for forward-planned IMRT. We also present results separately for all radiotherapy clinics and the subset of clinics that used IMRT in at least one breast cancer patient during the period of our study and treated at least 30 patients during the study period.

Table 6: Receipt of IMRT by tumor laterality and practice setting

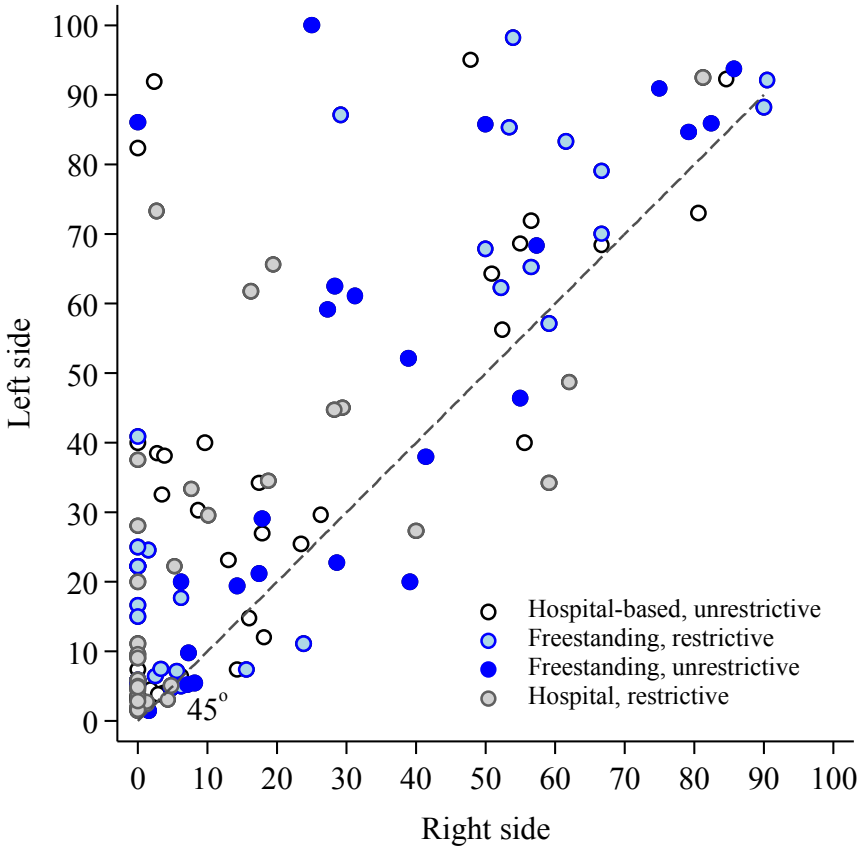
	All			Carrier IMRT coverage policy					
				Unrestrictive			Restrictive		
	Left	Right	Diff.	Left	Right	Diff.	Left	Right	Diff.
				All radiology groups					
Freestanding (%)	34	25	9	39	31	8	32	22	9
Hospital based (%)	15	9	6	29	20	9	10	5	5
Difference	19	16	3	10	12	-1	22	17	5
N	20,205			6,321			13,884		
	Groups that treated ≥30 patients and used IMRT for breast cancer								
Freestanding (%)	44	32	12	47	38	9	42	28	13
Hospital based (%)	25	16	9	42	30	12	17	9	8
Difference	19	16	3	5	8	-3	25	19	6
N	10,761			3,647			7,114		

Patients in both freestanding and hospital-based clinics with left-sided tumors are more likely to receive IMRT. The difference in the receipt of IMRT between women with left- and right-side tumors is actually larger in freestanding centers, but the difference of differences, 3 percentage points, become smaller and non-significant after adjusting for other patient characteristics. Among patients treated in groups that used IMRT for breast cancer (the lower panel), 32% of women with right-sided tumors treated in freestanding groups received IMRT compared to only 25% of women with left-sided tumors treated in hospital-based clinics.

IMRT treatment rates are substantially lower in areas with restrictive coverage policies. It is unclear if carriers effectively reduce the use of IMRT or if differences reflect how providers bill for IMRT (carriers in restrictive coverage areas do not allow providers to use IMRT billing codes for forward-planned IMRT) or unobserved differences between regions. The use of brachytherapy, another costly technology with unproven benefits, is similar between regions with restrictive and restrictive coverage policies (11% for both), suggesting that unobserved differences do not explain all of the difference in the use of IMRT. Restrictive coverage policies, which appear to single out right-sided tumors as an instance where IMRT is "rarely if ever" necessary, appear to differentially suppress the use of IMRT in women with right-sided tumors.

Averages mask important differences between clinics in their use of IMRT. Figure 5 shows radiology clinic-level IMRT rates for women with left- and right-side tumors. Each dot represents a clinic. The sample is limited to clinics that used IMRT in at least one breast cancer patient and treated at least 30 patients over the study period. In addition to clinics that do not use IMRT in breast cancer patients (not shown), there appear to be three groups of clinics: 1) clinics that use IMRT in women with left-side tumors but not right-side tumors (as indicated the cluster of dots along the y-axis), 2) clinics that mostly use IMRT in women with left-side tumors (the dots that lie above the 45-degree line), and 3) clinics that use IMRT in women with left- and right-side tumors in equal proportions (dots that lie along the 45-degree line). Casual inspection suggests that freestanding clinics are disproportionally represented among the subset of clinics in group 3.

Figure 5: Radiology group-level IMRT rates



The sample includes radiology groups that treated at least 30 breast cancer patients over the study period and used IMRT in at least one.

Conclusions

Personalized medicine has the potential to reduce costs and permit physicians to better match patients and treatments. Tumor laterality is not a diagnostic test, but, like many highly-touted personalized medicine tests, it groups patients based on their ability to benefit from a treatment. Because it is readily observable, we can study how laterality affects treatment decisions without having to worry about physicians' up-front decision to obtain the information in the first place.

Consistent with prior studies, we find that patients treated in freestanding clinics are substantially more likely to receive IMRT, suggesting that treatment decisions are being influenced by physicians' ability to profit from IMRT. We also find that while women with right-side tumors are less likely to receive IMRT compared to women with left-side tumors in freestanding clinics, they still receive IMRT at much higher rates than women with left-side tumors treated in hospital-based clinics. These results highlight the challenge of maximizing the benefit of tests that imperfectly predict patients' ability to benefit from a treatment in an environment where physicians' compensation is tied to the volume of treatments they provide.

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