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PERSONALIZED MEDICINE WHEN PHYSICIANS INDUCE DEMAND

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Personalized Medicine When Physicians Induce Demand
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ABSTRACT

Advocates for “personalized medicine” tests claim they can reduce health care spending by identifying patients unlikely to benefit from costly treatments. But most tests are imperfect, and so physicians have considerable discretion in how they use the results. We show that when physicians face incentives to provide a treatment, the introduction of an imperfect prognostic test will increase treatment rates. We study the interaction of incentives and information in physicians’ choice between conventional radiotherapy and intensity modulated radiation therapy (IMRT) for Medicare patients with breast cancer. IMRT is far more costly. Patients with left-side tumors are more likely to benefit from IMRT, though it is unnecessary for the vast majority of patients. IMRT use is 18 percentage points higher in freestanding clinics, where physician-owners share in the lucrative fees generated by IMRT, than in hospital-based clinics. Patients with left-side tumors are more likely to receive IMRT in both types of clinics. However, IMRT use in patients with right-side tumors (the low benefit group) treated in freestanding clinics is actually higher than use in patients with left-side tumors (high benefit group) treated in hospital-based clinics. Prognostic information affects use but does nothing to counter incentives to overuse IMRT.

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Introduction

Advances in genetics and artificial intelligence promise to launch an era of “personalized medicine.” Diagnostics and algorithms will help doctors distinguish between patients who are and are not likely to benefit from a treatment. Discussions of the impact of personalized medicine on treatment patterns and costs often proceed as if physicians will use information in a socially optimal manner. For example, proponents of personalized medicine claim it will reduce health care spending (for example, PhRMA 2015; Food and Drug Administration 2013) by identifying patients unlikely to benefit from costly therapies. However, physicians often face incentives to provide costly treatments. Further complicating matters, many tests do not definitively identify patients who will and will not benefit from a treatment. Instead, they provide another prognostic factor to consider alongside the standard clinical variables (Hunter et al. 2016).

In this paper we consider how physicians’ incentives and information on patients’ ability to benefit from treatment interact to shape treatment decisions. Using the standard physician-induced demand model, we show that the introduction of a test that predicts patients’ ability to benefit from treatment will lead to an increase in the share of patients receiving it. Also, treatment rates for patients most likely to benefit from treatment will be more responsive to incentives.

We evaluate the interaction between incentives and patients’ ability to benefit using the case of intensity modulated radiation therapy (IMRT) for breast cancer. Physicians differ in their incentives, based on whether they practice in a freestanding or hospital-based clinic. Patients differ in their ability to benefit from IMRT, based on whether the tumor is in the left or right breast. Patients with left-side tumors are more likely to benefit from IMRT.

A problem with studying the impact of personalized medicine tests on treatment is that most are not routinely ordered. Thus, it is only possible to observe the impact of test results on treatment for a selected subsample of patients. In the case of IMRT, physicians observe tumor laterality for all patients. Tumor laterality is also as good as randomly assigned in terms of being uncorrelated with education, income, or other factors related to patients’ receipt of advanced technology. We can study how laterality affects treatment decisions without having to consider physicians’ initial decision to obtain the information or its relation to other prognostic variables.

We find that IMRT use is much higher among women treated at freestanding clinics. Physicians at freestanding and hospital-based clinics vary their use of IMRT based on tumor laterality. However, use of IMRT among patients with right-side tumors (low benefit) treated in freestanding clinics is higher than the use of IMRT among patients with left-side tumors (high benefit) treated in hospital-based clinics, suggesting that incentives exert a powerful influence on treatment thresholds in this setting. Also, consistent with theory, differences in the use of IMRT between patients treated in freestanding and hospital-based clinics are larger, though non-significant, for patients with left-side tumors. The implication is that the introduction of personalized medicine tests will not necessarily reduce costs, and decisionmakers should evaluate the potential impact and cost savings from personalized medicine tests in light of the incentives facing the physicians who will act on the information.

In related work, Dinan et al. (2015) report that receipt of the 21-gene recurrence score assay, a test that predicts breast cancer patients' ability to benefit from chemotherapy, did not reduce the use of chemotherapy among breast cancer patients. However, only 10% of the patients in the sample received the test, making it difficult to independently identify the impact of the test because the physicians who ordered it may favor a more aggressive treatment approach.

A model of treatment choice

We modify the standard physician-induced demand model to show how allowing physicians to set different inducement levels for different patient groups affects the overall inducement rate and how financial incentives influence the relative inducement rates in each group.

To review, in the standard model physician utility is a function of income and the level of inducement: $u(y, i)$. Inducement raises income via its impact on the share of patients treated, but physicians pay a psychic cost for acting against their best assessment of patient and societal welfare. For simplicity, we assume physicians' labor supply is fixed. Income is $y = rx(i)$, where r is the reimbursement rate and $x(i)$ describes how the share of patients treated varies with inducement. Partial derivatives (McGuire and Pauly 1991) are $u_y > 0$, $u_{yy} < 0$; $u_i < 0$, $u_{ii} < 0$; and, $x_i > 0$, $x_{ii} = 0$. We assume additive separability: $u_{yi} = 0$

Assume there are two patient types who differ in their ability to benefit from treatment. The benefits of treatment vary within these groups, and so the disutility of inducing demand varies within each group. Physicians' utility for high-benefit types is $u^H(y, i)$. Physicians' utility for low-benefit types is $u^L(y, i)$, where

$$u^H(y, 0) = u^L(y, 0)$$

and the disutility of inducing demand among low-benefit patients is larger (i.e., more negative) and decreases at a faster rate:

$$u_i^L < u_i^H < 0,$$

$$u_{ii}^L < u_{ii}^H < 0.$$

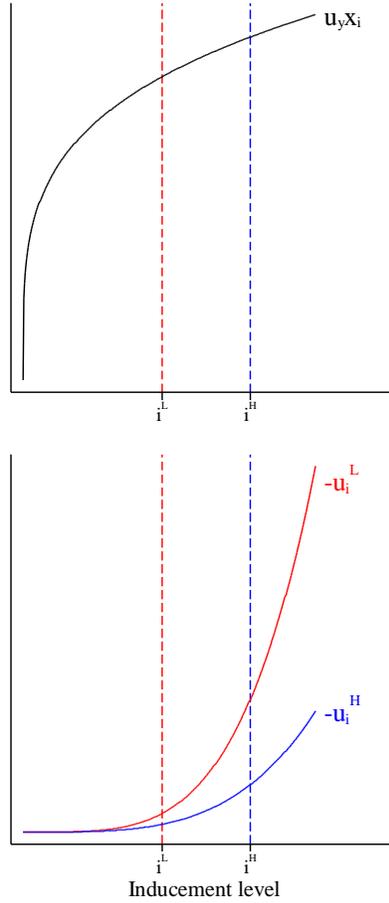
Physicians' marginal utility of income and the relationship between inducement and income, $x(i)$, do not vary by patient type.

If physicians can set different inducement levels for high- and low-benefit patients, the utility-maximizing inducement level is higher for high-benefit patients: $i^H \geq i^L$. To see this, note that the utility-maximizing inducement for low-benefit patients is defined by $u_y x_i = -u_i^L$ (see Figure 1). At the utility-maximizing level of inducement for low-benefit patients, the marginal utility of income exceeds the marginal utility of inducement for high-benefit patients,

$$u_y x_i(i^L) = -u_i^L(i^L) > -u_y^H(i^L).$$

Since physician utility for high-benefit patients is increasing at i^L , then $i^H \geq i^L$.

Figure 1: Utility maximizing inducement levels



If physicians cannot distinguish between high- and low-benefit patients, they maximize $\frac{1}{2}u^H(y, i) + \frac{1}{2}u^L(y, i)$, assuming that half of patients are each type. Let i^M indicate the level of inducement that maximizes this sum.

A test that allows physicians to distinguish between high- and low-benefit patients will cause average inducement levels (and, by extension, the share of patients receiving the treatment) to rise: $\frac{1}{2}i^L + \frac{1}{2}i^H > i^M$. To see this, note that i^M will fall in the interval between i^L and i^H and is defined by

$$u_y x_i + u_i^H = -[u_y x_i + u_i^L].$$

Since $u(\cdot)$ is single-peaked, utility for low-benefit patients (the term in the brackets on the right) is declining for $i > i^L$ and utility for high-benefit patients (the term on the left) is increasing for $i < i^H$. In the interval between i^L and i^H physicians' marginal utility for low-benefit patients decreases at a faster rate than physicians' marginal utility for high-benefit patients increases because $u_{ii}^L < u_{ii}^H < 0$ for all i . Therefore, physicians' marginal utilities for high- and low-benefit patients must intersect (which defines i^M) at a point in the interval between i^L and $\frac{1}{2}i^L + \frac{1}{2}i^H$, i.e. $\frac{1}{2}i^L + \frac{1}{2}i^H > i^M$.

The impact of a change in the reimbursement rate on inducement is ambiguous. If the income effect is strong enough, an increase in reimbursement rates could lead to a decrease in inducement. Regardless of whether an increase in the reimbursement rate increases or decreases inducement, inducement levels for high-benefit patients are more responsive to fee levels (when physicians can set separate inducement levels). The terms u_{ii}^H and u_{ii}^L enter positively in the denominators of the derivatives of i^H and i^L with respect to the reimbursement rate (see equation 2 in McGuire and Pauly). The denominator will be larger in absolute terms, and the derivative smaller, for low-benefit patients since $u_{ii}^L < u_{ii}^H$.

For the sake of simplicity and tractability, we assumed that physicians' utility for high-benefit patients does not depend on the inducement rate for low benefit patients and vice versa. There are two ways in which they may interact. First, the disutility of inducing demand for high-benefit patients may depend on the level of inducement for low-benefit patients. Following McGuire and Pauly, who model how physicians chose treatment rates when there are two payers, we assume they are independent. Second, an increase in the inducement level for low benefit patients will affect income and the marginal benefit of additional inducement for high-benefit patients via its impact on income. We ignore this second-order effect.

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 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.

Randomized trials comparing IMRT to conventional radiotherapy in breast cancer patients (Mukesh et al. 2013; Pignol et al. 2008) have found that IMRT reduces the rate of cosmetic side effects and self-limiting skin peeling and irritation. However, there are no differences in 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: “While IMRT may be of benefit in select cases where the anatomy is unusual, its routine use has not been demonstrated to provide significant clinical advantage.” 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, which is closer to the heart, and 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 increased use of relatively inexpensive techniques and technologies, like breath-holding or shields, has probably reduced the exposure of the heart to radiation (Recht 2017).

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. Hospital-based clinics may be staffed by employed radiation oncologists or radiation oncologists in independent groups.

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. 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 IMRT 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 cover average costs, including the cost of acquiring IMRT equipment. The difference between average and marginal costs may be especially large for capital-intensive services like IMRT. By comparison, the fee for treatment delivery of conventional beam radiation therapy is around \$100.

Radiation oncologists who have an ownership stake in a freestanding clinic receive a share of the group's profits, which are generated by the provision of services like IMRT that have large facility fees. Radiation oncologists who practice in hospital-based clinics do not. (It would be illegal under Medicare anti-kickback regulations for hospitals to give them a bonus based on the facility fees they generate.) For this reason, physicians in freestanding clinics face extra incentives to provide IMRT compared to physicians in hospital-based clinics.

Previous studies have found that prostate cancer patients treated by urology groups that acquire IMRT equipment (Bekelman et al. 2013; Carreyrou and Tamman 2010; General Accounting Office 2013; Mitchell 2013) and breast cancer patients treated in freestanding clinics are more likely to receive IMRT (Roberts et al. 2013; Smith et al. 2011). 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, Nallamothe et al. 2007; Shreibati and Baker 2012). These results 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. 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 important respects from that of previous studies of physician ownership. Most previous studies examine changes or differences in the volume of a particular procedure. Changes may reflect specialization. In our case, all patients receive treatment, either IMRT or another form of radiotherapy. Radiation oncologists may specialize by tumor site but do not specialize by treatment modality. Also, it is safe to assume that by the start of our study period, 2008, all radiation therapy clinics had the capability to perform IMRT, even if they never used it in breast cancer patients. Differences in use between freestanding and hospital-based clinics are not attributable to differences in the convenience or availability of IMRT.

Data

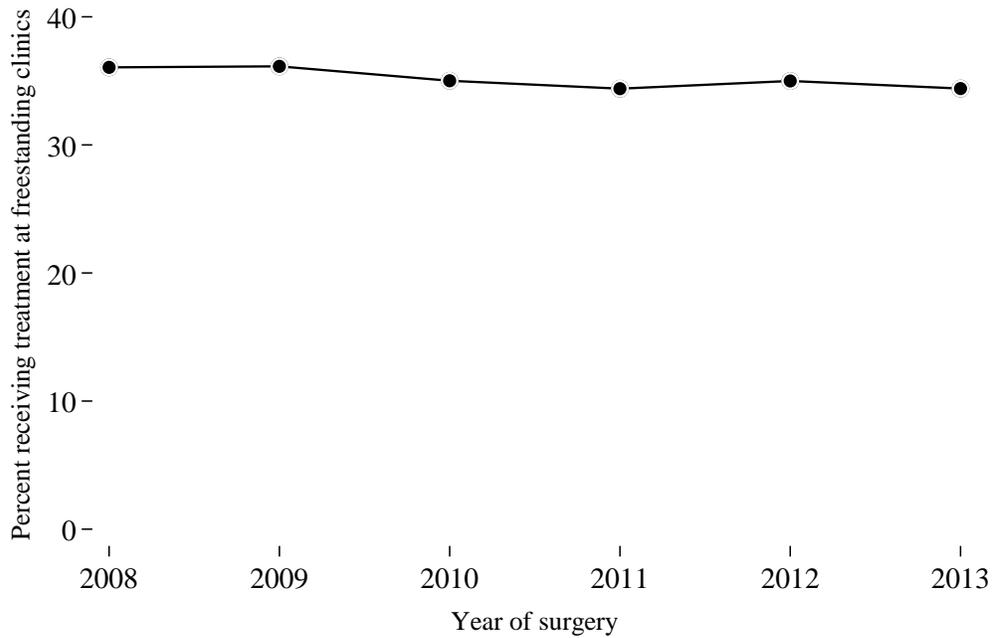
Using SEER-Medicare data, we estimate the impact of clinic type (freestanding versus hospital-based) and tumor laterality on the receipt of IMRT. SEER-Medicare includes tumor registry records from regional SEER tumor registries linked with Medicare claims for Medicare-eligible beneficiaries. The SEER 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 2008 and 2013 (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.

Table 1: Sample construction

Included	Excluded	Criteria
37,347		Had breast conserving surgery within 90 days of diagnosis between 2008 and 2013
29,010	8,337	Had a claim for radiotherapy
23,285	5,725	Age ≥ 66 and continuously enrolled in Medicare
23,252	33	Stage at diagnosis known
23,123	129	Early or regional stage (non-metastatic)

The primary outcome is the receipt of IMRT versus another form of radiation therapy. The primary independent variable is provider type. We classified a patient as receiving treatment at a freestanding clinic if her initial radiotherapy claim appeared in the National Claims History file (freestanding clinics bill as physician offices). All other patients were classified as treated at hospital-based clinics, which bill as hospital outpatient departments. We used a similar approach to categorize the type of provider where the patient received surgery. Figure 2 shows that the share of patients receiving treatment at freestanding clinics did not change over the study period.

Figure 2: The share of patients treated at freestanding clinics

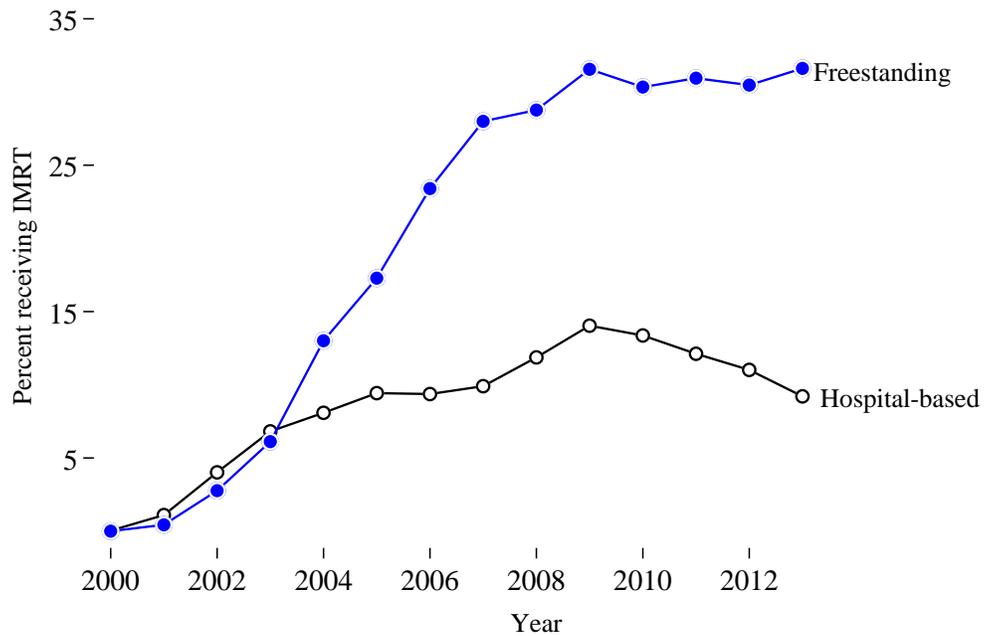


Trends in treatment patterns

Figure 3 shows the proportion of patients receiving IMRT by provider type. For this descriptive analysis, we include women diagnosed after 2000.

Initially, patients in hospital-based clinics were slightly more likely to receive IMRT. However, by 2008, 29% of patients treated in freestanding clinics received IMRT compared with only 12% percent of patients treated in hospital-based clinics.

Figure 3: The share of patients receiving IMRT



Patients who did not receive IMRT either underwent conventional beam radiation or brachytherapy. Brachytherapy requires the implantation of a catheter to deliver the radioactive seeds. In breast cancer patients the implantation typically occurs during surgery, which precedes radiotherapy, and so radiation oncologists have less influence over the use of brachytherapy. The share of patients receiving brachytherapy was 10.6% in freestanding clinics and 10.4% in hospital-based clinics.

Regression-adjusted differences

We estimated a probit regression to measure differences in the receipt of IMRT between freestanding and hospital-based clinics, adjusted for observable patient characteristics. Table 2 presents sample means of the variables included in the model. 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.

Table 2: Patient characteristics

	All patients	Radiotherapy clinic type		P-value
		Freestanding	Hospital	
		%		
Freestanding clinic	35.2	100.0	0.0	
Left-side tumor	50.6	50.2	50.8	0.34
Tumor size >2 cm	22.5	22.9	22.2	0.21
Positive lymph nodes	15.6	15.9	15.4	0.39
Local stage	83.3	82.9	83.5	0.24
ER positive	86.4	85.2	87.0	<0.01
Age				0.49
65-74	56.0	56.5	55.7	
75-84	37.7	37.3	37.9	
85+	6.3	6.2	6.4	
Race				<0.01
White	88.1	88.5	87.9	
Black	6.4	5.6	6.9	
Asian	1.9	2.0	1.8	
Hispanic	1.1	1.2	1.0	
Other	2.5	2.7	2.4	
Region				<0.01
Pacific	38.6	45.6	34.8	
East	43.8	38.3	46.8	
North	11.5	9.1	12.8	
Other	6.1	7.1	5.7	
Medicaid coverage	8.8	9.7	8.4	<0.01
Rural/less urban	12.3	14.0	11.4	<0.01
Year				0.41
2008	16.6	17.1	16.4	
2009	17.0	17.5	16.8	
2010	16.8	16.7	16.8	
2011	17.0	16.7	17.2	
2012	16.4	16.3	16.5	
2013	16.1	15.8	16.3	
N	23,123	8,132	14,991	

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 are 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 coefficients on the other variables are small and non-significant.

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)	**	0.17	(0.03, 0.32)	*	0.16	(0.03, 0.30)	*
Left-side tumor	0.07	(0.05, 0.09)	**	0.08	(0.06, 0.10)	**	0.08	(0.06, 0.10)	**
Tumor size >3 cm	0.00	(-0.02, 0.01)		0.00	(-0.01, 0.02)		0.01	(-0.01, 0.03)	
Positive lymph nodes	0.00	(-0.05, 0.05)		0.00	(-0.05, 0.04)		0.00	(-0.05, 0.05)	
Local stage	-0.01	(-0.06, 0.03)		-0.02	(-0.07, 0.02)		-0.02	(-0.07, 0.03)	
ER positive	0.00	(-0.02, 0.02)		0.01	(-0.01, 0.02)		0.01	(-0.01, 0.03)	
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)		0.00	(-0.03, 0.02)		-0.01	(-0.03, 0.02)	
Black	0.03	(-0.01, 0.07)	+	0.05	(0.01, 0.08)	**	0.04	(-0.00, 0.08)	+
Asian	-0.03	(-0.08, 0.02)		-0.08	(-0.15, -0.01)	*	-0.06	(-0.14, 0.01)	+
Hispanic	-0.03	(-0.11, 0.04)		-0.06	(-0.12, 0.00)	+	-0.05	(-0.12, 0.02)	
Other	-0.04	(-0.09, 0.01)		-0.07	(-0.13, -0.02)	**	-0.08	(-0.14, -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, -0.00)	*	-0.07	(-0.12, -0.01)	*
2009	0.02	(0.00, 0.05)	*	0.02	(0.00, 0.05)	*	0.02	(-0.00, 0.04)	+
2010	0.02	(-0.01, 0.04)		0.02	(-0.01, 0.04)		0.01	(-0.02, 0.03)	
2011	0.01	(-0.02, 0.04)		0.01	(-0.02, 0.04)		0.00	(-0.03, 0.03)	
2012	0.00	(-0.03, 0.04)		0.00	(-0.03, 0.04)		-0.01	(-0.04, 0.03)	
2013	-0.01	(-0.04, 0.03)		-0.01	(-0.04, 0.03)		-0.02	(-0.05, 0.02)	
N	23,123			23,123			19,092		

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

We estimated an instrumental variables model to confirm that differences in the receipt of IMRT are not biased by unobserved patient characteristics. We used 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 received surgery in hospitals with radiation oncology clinics were more likely to receive radiotherapy at a hospital-based clinic.

The identifying assumption is that the characteristics of patients that determine the type of facility at which they receive surgery are unrelated to the factors that determine whether they receive IMRT, conditional on radiotherapy clinic type. 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. To the extent that patients with unusual tumor anatomy are more likely to be referred to a particular type of facility, they are probably more likely to go to a large hospital that has an onsite radiotherapy clinic. However, limiting the sample to women undergoing breast conserving surgery reduces variation in tumor anatomy.

Figure 3 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 4 and 3 percentage points more likely to receive post-operative radiotherapy. However, these differences are small in percentage terms given that 78% of patients receive post-operative radiotherapy.

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

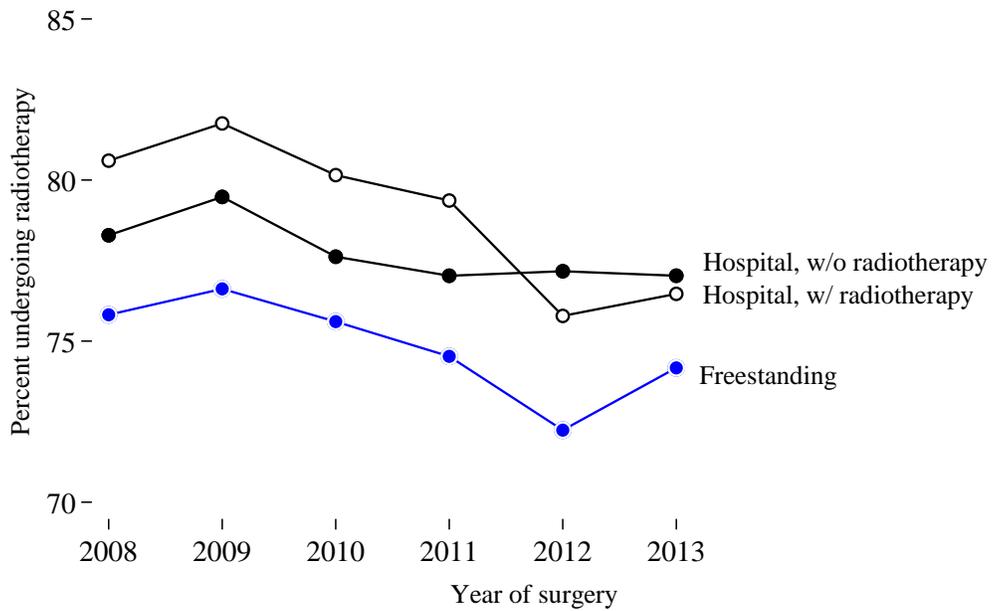


Table 4 shows patient characteristics by surgery provider type (as opposed to radiation therapy provider type). Patients treated at freestanding and hospital-based clinics look fairly similar, at least based on observable characteristics. What differences do exist suggest that patients in freestanding clinics have worse prognoses. However, the tumor characteristic that is most closely related to patients' ability to benefit from IMRT, tumor laterality, does not differ.

Table 4: Patient characteristics by surgery provider type

	Surgery provider type			P-value
	Freestanding	Hospital without radiotherapy %	Hospital with radiotherapy	
Left-side tumor	50.3	50.8	50.5	0.85
Tumor size >3 cm	25.2	22.1	21.4	<0.01
Positive lymph nodes	20.8	14.2	15.0	<0.01
Local stage	77.8	84.7	83.8	<0.01
ER positive	85.4	87.3	85.0	<0.01
N	4,031	6,066	13,026	

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, 39.1% receive radiotherapy in a freestanding clinic. Among patients receiving surgery in hospitals without a radiotherapy clinic, 68.3% received radiotherapy in a freestanding clinic compared to only 18.5% of patients who received surgery in a hospital with a radiotherapy clinic. Patients treated at hospitals without radiotherapy centers are more likely to receive IMRT, reflecting the fact that 68.3% received radiotherapy in freestanding clinics. Conditional on radiotherapy clinic type, IMRT use is similar across surgery provider types, providing support for the validity of surgery setting as an instrument.

Table 5: Receipt of IMRT by surgery provider type

Radiotherapy facility	All	Surgery provider type		
		Free-standing	Hospital without	Hospital with
Freestanding clinic	35.2%	39.1%	68.3%	18.5%
IMRT	18.5%	17.3%	25.6%	15.6%
IMRT by provider type				
Freestanding	30.6%	29.0%	31.8%	29.6%
Hospital	12.0%	9.8%	12.2%	12.4%
N	23,123	4,031	6,066	13,026

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 assessed 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. The F-statistic associated with the instrument is 152. Results from the IV probit model are similar to those from the baseline model.

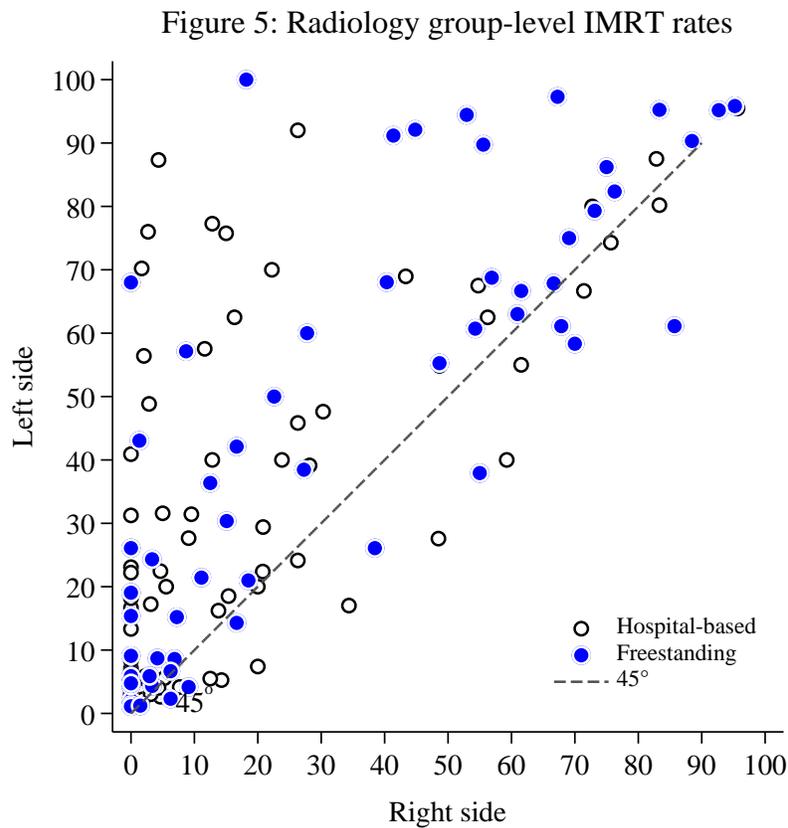
The third set of regression results are from an IV probit model estimated on the subsample of patients who received surgery at hospitals, where observable patient characteristics are similar between hospitals with and without radiotherapy clinics. Marginal effects are similar to those from the other models.

Following David and Neuman (2011), we also examined differences in the use of IMRT by facility type among physicians who practice in both types. Among the 998 physicians who treated at least 5 patients over the study period, there are 78 who treated at least 20% but no more than 80% of their patients in freestanding clinics. We term these physicians “splitters,” reflecting the fact that they treated patients in both settings. We estimated the impact of treatment setting on the likelihood of receiving IMRT among patients treated by splitters. Patients treated by splitters in freestanding clinics were 12 percentage points (95% CI: 5 to 19 percentage points)

more likely to receive IMRT. This result provides additional evidence that there is a causal relationship between clinic type and treatment.

Practice setting and personalized medicine

Figure 5 shows clinic-level treatment patterns by tumor laterality for clinics that treated at least 30 patients between 2008 and 2013. Circles above the 45 degree line indicate clinics where the share of patients with left-side tumors who received IMRT exceeds the share of patients with right-side tumors who received IMRT. There is substantial heterogeneity in clinic treatment patterns. Freestanding clinics seem to be disproportionately represented among clinics that have IMRT use rates above 50% and cluster around the 45 degree line.



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

Table 6: Differences in the use of IMRT by clinic type and tumor laterality

	Radiotherapy clinic type		Difference
	Freestanding	Hospital	
	%		
Right	26.1 (24.8, 27.5)	8.5 (7.8, 9.1)	17.6 (16.2, 19.1)
Left	35.1 (33.6, 36.5)	15.3 (14.5, 16.1)	19.7 (18.1, 21.4)
Difference	8.9 (7.0, 10.9)	6.9 (5.8, 7.9)	2.1 (-0.2, 4.3)

Table 6 shows unadjusted rates and differences in the use of IMRT by clinic type and tumor laterality. Physicians in both types of clinics personalized medicine, in the sense that patients with left-side tumors were more likely to receive IMRT. However, patients were more likely to receive IMRT if they were treated in a freestanding clinic, regardless of tumor type. In fact, patients with right-sided tumors in freestanding clinics were more likely to receive IMRT compared to patients with left-sided tumors treated in hospital-based clinics.

The difference in IMRT use between patients with left- and right-side tumors is 2.1 percentage points higher in freestanding clinics. The adjusted difference, from a probit model that includes an interaction between clinic type and tumor laterality, is 2.2 (-2.0 to 6.2) percentage points. The confidence interval is wide, but the point estimate is consistent with the prediction that treatment rates among high-benefit patients are more responsive to incentives

Figure 6: The share of patients receiving IMRT, by tumor laterality

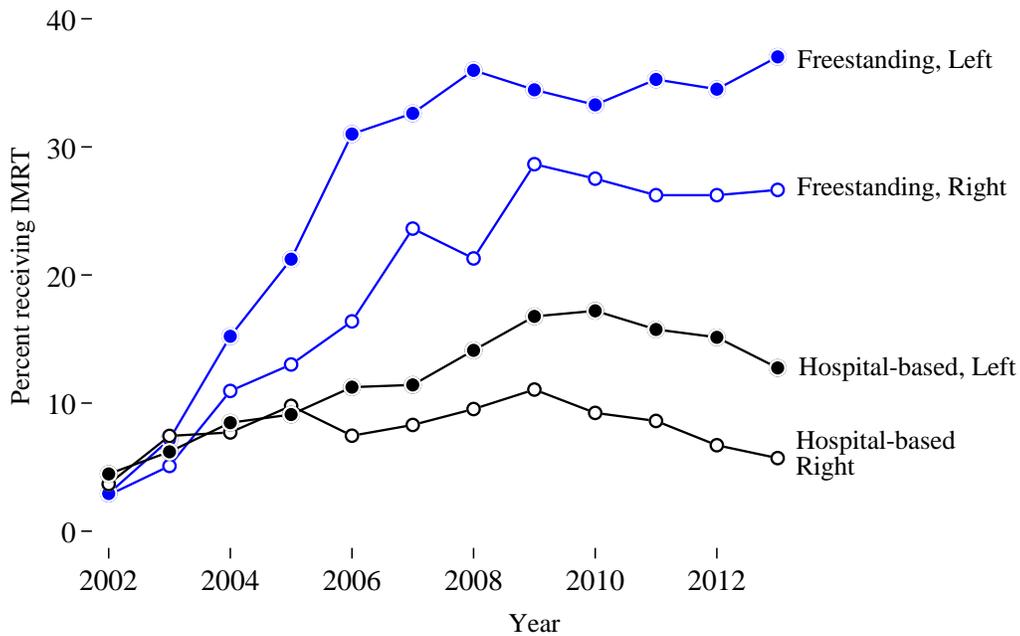


Figure 6 displays trends in the share of patients receiving IMRT by laterality. Interestingly, differences in the use of IMRT between patients with left- and right-side tumors grew larger over time, at least until 2009. This contrasts with typical patterns of use of new technologies, where initially physicians use them in patients most likely to benefit and then gradually expand use to other patients. Physicians, especially ones in hospital-based clinics, appear to have become more discriminating over time. Perhaps these patterns reflect greater attention to cardiac-related morbidity from radiotherapy.

Conclusions

Personalized medicine has the potential to help physicians better match patients to treatments and reduce costs in the process. However, the effects of new tests and algorithms will depend on the financial incentives facing physicians. When physicians face incentives to induce demand, additional information may lead to higher levels of treatment. We cannot test the prediction directly, but the data are consistent with another prediction: that treatment rates in the high benefit patient group are more responsive to incentives.

Consistent with prior studies, we find that patients treated in freestanding clinics were significantly more likely to receive IMRT. Our instrumental variables analysis and analysis of treatment patterns by physicians who treat patients in both clinic types suggests that the relationship is causal.

We find that women with right-side tumors treated in freestanding clinics were more likely to undergo IMRT than women with left-side tumors treated in hospital based clinics. This result implies that payers will need to link coverage policies to the results of personalized medicine tests (and enforce these policies) if they hope to leverage personalized medicine to reduce overtreatment. Simply requiring that physicians perform the tests may be insufficient when tests are imperfect. Broadly speaking, our 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 linked to the volume or intensity of treatments they provide.

References

- American Society for Radiation Oncology. "Choosing Wisely. Five Things Physicians and Patients Should Question." 2013 <http://www.choosingwisely.org/wp-content/uploads/2015/02/ASTRO-Choosing-Wisely-List.pdf>
- Bekelman, Justin, Gita Suneja, Thomas Guzzo, Craig E. Pollack, Katrina Armstrong, and Andrew J. Epstein, 2013. "Effect of practice integration between urologists and radiation oncologists on prostate cancer treatment patterns." *Journal of Urology* 190(1), 97-101.
- Baker, Laurence C., 2010. "Acquisition of MRI Equipment by Doctors Drives up Imaging Use and Spending." *Health Affairs* 29, 2252-2259.
- Barro, Jason R., Robert S. Huckman, and Daniel P. Kessler, 2006. "The Effects of Cardiac Specialty Hospitals on the Cost and Quality of Medical Care." *Journal of Health Economics* 25, 702-21.
- Carreyrou, John, and Maurice Tamman, 2010. "A device to kill cancer, lift revenue." *Wall Street Journal*, December 7, 2010.
- David, Guy, and Mark Neuman, 2011. "Physician Division of Labor and Patient Selection for Outpatient Procedures." *Journal of Health Economics*, March 2011 30(2), 381-391.

Dinan, Michaela A., Xiaojuan Mi, Shelby D. Reed; et al, 2015. "Association Between Use of the 21-Gene Recurrence Score Assay and Receipt of Chemotherapy Among Medicare Beneficiaries With Early-Stage Breast Cancer, 2005-2009." *JAMA Oncology* 1(8), 1098-1109.

Food and Drug Administration. Paving the Way Personalized Medicine. October 2013. <https://www.fda.gov/downloads/scienceresearch/specialtopics/personalizedmedicine/ucm372421.pdf>

General Accounting Office. "Higher Use of Costly Prostate Cancer Treatment by Providers Who Self Refer Warrants Scrutiny." GAO-13-525. July 2013.

Hollenbeck, Brent K., John M. Hollingsworth, Rodney L. Dunn, Zaojun Ye, John D. Birkmeyer; FACS, 2010. "Ambulatory Surgery Center Market Share and Rates of Outpatient Surgery in the Elderly." *Surgical Innovation*, 17, 340-345.

Hollingsworth, John M., Zaojun Ye, Seth A. Strobe, Sarah L. Krein, Ann T. Hollenbeck, and Brent K. Hollenbeck, 2010a. "Physician-Ownership of Ambulatory Surgery Centers Linked to Higher Volume of Surgeries." *Health Affairs*, 29, 683-689.

Hollingsworth, John M., Sarah L. Kreindg, John D. Birkmeyer, Zaojun Ye, Hyungjin M. Kim, Yun Zhang, and Brent K. Hollenbeck, 2010b. "Opening of Ambulatory Surgery Centers and Rates of Stone Surgery in Healthcare Markets." *Journal of Urology*, 184, 967-971.

Hollenbeck, Brent K., John M. Hollingsworth, Rodney L. Dunn, Zaojun Ye, John D. Birkmeyer; FACS, 2011. "Ambulatory Surgery Center Market Share and Rates of Outpatient Surgery in the Elderly." *Surgical Innovation*, 146, 187-193.

Hunter, David J., 2016. "Uncertainty in the era of precision medicine." *New England Journal of Medicine* 375, 711-713.

Iizuka, Toshiaki, 2007. "Experts' Agency Problems: Evidence from the Prescription Drug Market in Japan." *RAND Journal of Economics* 38, 844-862.

Iizuka, Toshiaki, 2012. "Physician Agency and Adoption of Generic Pharmaceuticals." *American Economic Review*, 102, 2826-2858.

McGuire, Thomas G., and Mark V. Pauly, 1991. "Physician response to fee changes with multiple payers." *Journal of Health Economics* 10(4), 385-410.

Mukesh, Mukesh B., Gillian C. Barnett, Jennifer S. Wilkinson, Anne M. Moody, Charles Wilson, Leila Dorling, Charleen Chan Wah Hak, Wendi Qian, Nicola Twyman, Neil G. Burnet, Gordon C. Wishart, and Charlotte E. Coles, 2013. "Randomized Controlled Trial of Intensity-Modulated Radiotherapy for Early Breast Cancer: 5-Year Results Confirm Superior Overall Cosmesis." *Journal of Clinical Oncology* 31(36), 4488-4495.

- Mitchell, Jean M., 2013. “Urologists’ use of intensity-modulated radiation therapy for prostate cancer.” *New England Journal of Medicine* 369(17), 1629-1637.
- Mitchell, Jean M., and Jonathan H. Sunshine, 1992. “Consequences of physicians’ ownership of health care facilities-joint ventures in radiation therapy.” *New England Journal of Medicine* 327(21), 1497-1501.
- Mitchell, Jean M., 2005. “Effects of Physician-Owned Limited Service Hospitals: Evidence from Arizona.” *Health Affairs* W5, 481-490.
- Mitchell, Jean M., 2008. “Do Financial Incentives Linked to Ownership of Specialty Hospitals Affect Physicians’ Practice Patterns?” *Medical Care* 46, 732-737.
- Mitchell, Jean M., 2010. “Effect of Physician Ownership of Specialty Hospitals and Ambulatory Surgery Centers on Frequency of Use of Outpatient Orthopedic Surgery.” *Archives of Surgery* 145, 732-738.
- Nallamothu, Brahmajee K., Mary A.M. Rogers, Michael E. Chernew; et al, 2007. “Opening of Specialty Cardiac Hospitals and Use of Coronary Revascularization in Medicare Beneficiaries.” *Journal of the American Medical Association* 297, 962-968.
- Noridian. *Local Coverage Determination (LCD): Intensity Modulated Radiation Therapy (IMRT)*. (L34080) Accessed: December 15, 2015.
<https://med.noridianmedicare.com/documents/10534/5321625/Local+Coverage+Determination+for+Intensity+Modulated+Radiation+Therapy+%28IMRT%29%20%28L34080%29>
- PhRMA. *Value of Personalized Medicine*. Spring 2015.
http://www.phrma.org/sites/default/files/pdf/chart_pack-value_of_personalized_medicine.pdf
- Pignol, Jean-Philippe, Ivo Olivotto, Eileen Rakovitch, Sandra Gardner, Katharina Sixel, Wayne Beckham, Thi Trinh Thuc Vu, Pauline Truong, Ida Ackerman, and Lawrence Paszat. 2008. “A multicenter randomized trial of breast intensity-modulated radiation therapy to reduce acute radiation dermatitis.” *Journal of Clinical Oncology* 26(13), 2085-2092.
- Recht, Abram. 2017 “Radiation-Induced Heart Disease After Breast Cancer Treatment: How Big a Problem, and How Much Can—and Should—We Try to Reduce It?” *Journal of Clinical Oncology* 35:11, 1146-1148.
- Roberts, Kenneth B., Pamela R. Soulos, Jeph Herrin, James B. Yu, Jessica B. Long, Edward Dostaler, and Cary P. Gross, 2013. “The Adoption of New Adjuvant Radiation Therapy Modalities Among Medicare Beneficiaries with Breast Cancer: Clinical Correlates and Cost Implications.” *International Journal of Radiation Oncology Biology Physics* 85(5), 1186-92.
- Smith, Benjamin D., I-Wen Pan, Ya-Chen T. Shih, Grace L. Smith, Jay R. Harris, Rinaa Punglia, Lori J. Pierce, Reshma Jagsi, James A. Hayman, Sharon H. Giordano, and Thomas A. Buchholz,

2011. "Adoption of intensity-modulated radiation therapy for breast cancer in the United States."
Journal of the National Cancer Institute 103(10), 798-809.

Shreibati, Jacqueline B., and Laurence C. Baker, 2011. "The Relationship Between Low Back
Magnetic Resonance Imaging, Surgery, and Spending: Impact of Physician Self-Referral Status."
Health Services Research 46, 1362-1381.