

¹⁸F-Fluoride PET Used for Treatment Monitoring of Systemic Cancer Therapy: Results from the National Oncologic PET Registry

Bruce E. Hillner¹, Barry A. Siegel², Lucy Hanna³, Fenghai Duan³, Bruce Quinn⁴, and Anthony F. Shields⁵

¹Department of Internal Medicine and the Massey Cancer Center, Virginia Commonwealth University, Richmond, Virginia; ²Division of Nuclear Medicine, Mallinckrodt Institute of Radiology and the Siteman Cancer Center, Washington University School of Medicine, St. Louis, Missouri; ³Department of Biostatistics and Center for Statistical Sciences, Brown University School of Public Health, Providence, Rhode Island; ⁴Foley Hoag LLC, Boston, Massachusetts; and ⁵Karmanos Cancer Institute, Wayne State University, Detroit, Michigan

In a national prospective registry, we previously studied the impact of ¹⁸F-sodium fluoride PET (NaF PET) on the intended management of cancer patients with osseous metastases. The clinical impact of NaF PET for monitoring the response to systemic therapies in such patients is unknown. The objective of this study was to assess the impact of NaF PET results obtained for treatment monitoring of systemic cancer therapy. **Methods:** Before and after NaF PET, we collected prospective data from referring and interpreting physicians for cancer patients 65 y or older receiving systemic therapy (use of 1 or more categories including hormonal, chemotherapy, bisphosphonates, or immunotherapy). The analysis set consisted of 2,217 patients who underwent 2,839 scans (68% prostate, 17% breast, 6% lung, and 8% other cancers) ordered for treatment monitoring. Two or more categories of systemic therapy were planned in 56% of prostate and 43% of breast cancer patients. **Results:** The overall rates of prior radionuclide bone imaging were 78%, 76%, and 66% for prostate, breast, and other cancers, respectively. Fifty-seven percent of patients underwent prior NaF PET. Overall change in management associated with NaF PET was 40%. In patients with prior NaF PET scans for comparison, continuing current therapy was planned in 79% when scans showed no change or a decrease or absence of osseous metastasis. Treating physicians planned to switch therapy in 59% of patients after scans showed evidence of new or progressive metastasis. When an additional parameter, estimated prognosis, was worse, switching therapy was even more common (76%). **Conclusion:** The impact of NaF PET used for treatment monitoring was high in patients with evidence of progressive osseous metastasis. Most such patients had plans to switch to a new cancer-directed therapy.

Key Words: bone; oncology; breast; GU; PET/CT; breast cancer; positron emission tomography; prostate cancer; sodium fluoride PET; treatment monitoring

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Oncologists have many options for tracking a patient's response to cancer therapy, including various imaging modalities and tumor markers (1–3). Although there are multiple treatments for osseous metastatic disease, assessing treatment response is challenging because of the complex morphology of skeletal lesions and the difficulty in quantifying lesion volume. For patients with prostate and breast cancer, bone is often the dominant or only site of metastatic disease, and planar bone scintigraphy (BS) with ^{99m}Tc-phosphonates is a common imaging modality. BS provides a total skeletal survey at relatively low cost and has high sensitivity for detecting osteoblastic activity (4–6). However, BS has well-known limitations including being less sensitive for predominantly osteolytic lesions and limited specificity, with positive findings caused by benign lesions, prior trauma, and arthritis (4,7). The performance of conventional BS is improved by use of SPECT and SPECT/CT (4), but whole-body imaging with these methods is not currently standard practice.

A promising alternative to conventional BS is PET or integrated PET/CT with ¹⁸F-sodium fluoride (hereinafter collectively referred to as NaF PET). Advantages of NaF PET include superior image quality with improved sensitivity, lower radiation dose, higher bone uptake, and superior pharmacokinetics (a shorter time from injection to imaging and faster blood clearance) (8,9). When NaF PET is performed with PET/CT, as is now common, the direct correlation of PET and CT findings allows improved specificity, because many benign processes have characteristic CT appearances (10,11). Although the excellent performance of NaF PET for detection of osseous metastasis is well documented, including in comparison to conventional BS (12–17), its clinical impact when used to monitor treatment response is uncertain.

Since 2011, NaF PET has been available in the United States, under a Coverage with Evidence Development program, for Medicare beneficiaries with suspected or known osseous metastasis. For each scan, prospective data to assess the referring physician's intended management were collected with a questionnaire-based approach and submitted to the National Oncologic PET Registry (NOPR) (18). We have previously reported the impact of diagnostic NaF PET on intended management in men with prostate cancer and in patients with other types of cancer (19,20). We now report the impact of NaF PET in NOPR patients when used to assess response to systemic therapy for osseous metastatic disease.

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For correspondence or reprints contact: Bruce E. Hillner, 1101 East Marshall St., Rm. 7031, Virginia Commonwealth University, Richmond, VA 23298-0170.
E-mail: Hillner@vcu.edu
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MATERIALS AND METHODS

NOPR Design

NOPR was initially designed to assess the impact of PET with ^{18}F -FDG on intended cancer management. We have previously reported the impact of ^{18}F -FDG PET by cancer type and testing indication, including its use for monitoring cancer therapy (21–24). The NaF PET registry follows the basic design of the ^{18}F -FDG PET registry in that data were prospectively collected from the requesting physician before and after imaging. The interpreting physician, using a structured case report form, also recorded the NaF PET result. Our prior reports on ^{18}F -FDG PET and NaF PET include details on NOPR operations, human subject protections, and how data were collected. The research conducted using NOPR data is registered at ClinicalTrials.gov (#NCT00868582), and data forms are available on the NOPR website (<http://www.cancerpetregistry.org/>).

Treatment Monitoring

The NOPR case report forms for NaF PET included additional questions when the imaging indication was to “monitor tumor response to treatment during the planned course of therapy (i.e., when a change in therapy is anticipated).” Treatment was categorized by the category of systemic therapy (including chemotherapy, hormonal therapy, bisphosphonates, biologic response modifiers, or immunotherapy). We also collected results on those receiving radiotherapy but did not include those in this analysis because fewer than 10% received such treatment. The specific drugs or combinations of systemic therapies were not collected nor was a history of prior cancer-directed therapies. Before NaF PET, the plan for treatment was recorded in response to the following question: if you were to continue your patient’s management without doing any other testing first (e.g., PET, CT, MR imaging, biopsy), what would be your treatment plan today?

- Continue and complete currently ongoing therapy
- Modify dose or schedule of currently ongoing therapy
- Switch to another therapy or add another mode of therapy
- Stop therapy and switch to supportive care

After the PET results were available, the referring physician recorded the post-PET plan for treatment using the same 4 options. Additionally, before and after NaF PET, the referring physician recorded his or her impression of the patient’s therapy response and prognosis.

The interpreting physician recorded whether prior radionuclide bone imaging (BS or NaF PET) was available for comparison, along with the date of the prior study. NaF PET findings were categorized as normal or benign versus equivocal, probable, or definite osseous metastasis. Osseous metastatic disease was further characterized as unifocal, multifocal, or diffuse. If prior BS or NaF PET was available, the comparison was categorized as showing no evidence, resolution, or reduction of metastasis; no change; or progression or new sites of osseous metastasis.

Analysis Plan and Cohort

The endpoint of greatest interest was the modification of the treatment (22). Changes were defined as a binary variable at the scan level, and multiple scans collected from the same patient were assumed to be independent observations. In addition to the routine descriptive statistics (e.g., mean, frequency), Pearson χ^2 tests were used to assess the association between each pre-PET profile characteristic and the cancer type, as shown in Table 1. For the significance of the associated pre-PET profile characteristics, a post hoc analysis with a Bonferroni adjustment for multiple comparisons was conducted to identify which category of that characteristic performed differently across various cancer types.

An a priori statistical plan for all registry indications of NaF PET was based on an anticipated rate of change in intended management of 15% and a sample size of 13,040 cases for all imaging indications (prior reports show the impact of NaF PET on initial staging, suspected first osseous metastasis, and suspected progression of osseous metastasis (19,20)). To compare the pre- and post-PET therapeutic plans, a logistic regression model was fit to assess differences of change in management across different cancer types. All tests were 2-sided, and a *P* value threshold of 0.05 (or the Bonferroni-adjusted threshold for tests needing correction for multiple comparisons) was used to declare statistical significance. All statistical analyses were performed using SAS 9.3 (SAS Institute) or R (version 2.15.3; R project, <http://www.r-project.org/>) software as previously reported (19,20).

Final protocol revisions were implemented on January 27, 2012, and we report on the patient cohort from that date through June 30, 2014. The analysis was conducted at this time to coincide with submission, by the NOPR investigators, of data through this date to the Center for Medicare and Medicaid Services as part of a reconsideration request to modify the National Coverage Decision to end the prospective data collection requirements and provide Medicare coverage of NaF PET.

In this report, we excluded patients younger than 65 y (7.6%), thus limiting our analyses to the traditional Medicare age range.

RESULTS

Cohort Profile

Table 1 shows the cohort profile. The final dataset included 2,839 scans done in 2,217 patients; of these, 1,779 patients underwent a single scan for treatment monitoring, 320 underwent 2, 76 underwent 3, and 42 underwent 4 or more. Of the 1,779 patients undergoing a single NaF PET scan for treatment monitoring during the study interval (January 2012 to June 2014), 779 patients (*n* = 44%) underwent a prior NaF PET scan and 427 (*n* = 24%) underwent a prior conventional BS scan. Of the 2,839 scans, 1,940 were obtained for prostate (68.3%), 476 for breast (16.8%), 185 for lung (6.5%), and 238 for other cancer types (8.4%). The median patient age was 75 y (25%–75% quartiles, 70–80 y). PET/CT scans comprised 94.6% of the total number of scans, and 5.4% were PET only.

The clinical evidence prompting imaging was often an elevated or rising tumor marker, occurring as the sole indication in 38.2% of patients and in conjunction with bone pain in 22.7%. Approximately 45% of patients had bone pain with similar rates across cancer types. About 5% had evidence of metastases on other imaging studies.

Most patients had metastatic disease. Patient summary stage was judged by referring physicians before NaF PET to be multifocal metastatic disease in 59% overall, slightly lower in prostate and slightly higher in the other cancers. About 4% were in remission with no evidence of disease, and about 10% had local or regional disease, but we did not ask whether patients had been receiving adjuvant therapy. Referring physicians did not commit to a specific stage in 18% of patients.

For patients with plans to continue current therapy, the category of systemic therapy was inferred. In prostate cancer patients, 75% of plans included hormonal therapy, 49% chemotherapy, 42% bisphosphonates, and 19% immunotherapy. Combinations of 2 or more categories were predominant. Hormonal or chemotherapy as the sole systemic therapy was planned in 21% and 14% of patients, respectively. Among breast cancer patients, plans included chemotherapy in 77% and hormonal therapy in 47%.

TABLE 1
Pre-PET Profile of Treatment Monitoring of Systemic Therapy

Patient characteristic and pre-PET profile	Prostate	Breast	Lung	Other	Combined	Difference between cancer types χ^2 P^*
Total scans (% of cohort)	1,940 (68.3)	476 (16.8)	185 (6.5)	238 (8.4)	2,839 (100)	
Clinical manifestations at the time of NaF PET						$P < 0.0001$
Elevated or rising tumor markers [†]	709 (36.5)	181 (38.0)	94 (50.8)	101 (42.4)	1,085 (38.2)	
Bone pain	583 (30.1)	45 (9.5)	3 (1.6)	13 (5.5)	644 (22.7)	
Bone pain and rising tumor marker(s)*	314 (16.2)	164 (34.5)	57 (30.8)	92 (38.7)	627 (22.1)	
Other imaging findings	109 (5.6)	27 (5.7)	10 (5.4)	11 (4.6)	157 (5.5)	
Other evidence	170 (8.8)	39 (8.2)	8 (4.3)	12 (5.0)	229 (8.1)	
None	55 (2.8)	20 (4.2)	13 (7.0)	9 (3.8)	97 (3.4)	
Pre-PET summary stage (%)						$P < 0.0001$
No evidence of disease	73 (3.8)	38 (8.0)	7 (3.8)	10 (4.2)	128 (4.5)	
Local	160 (8.2)	8 (1.7)	15 (8.1)	15 (6.3)	198 (7.0)	
Regional	53 (2.7)	6 (1.3)	16 (8.6)	1 (0.4)	76 (2.7)	
Single distant metastases	168 (8.7)	54 (11.3)	20 (10.8)	26 (10.9)	268 (9.4)	
Multiple distant metastases	1,082 (55.8)	311 (65.3)	118 (63.8)	159 (66.8)	1,670 (58.8)	
Unknown	404 (20.8)	59 (12.4)	9 (4.9)	27 (11.3)	499 (17.6)	
Pre-PET suspected response (%)						$P < 0.0001$
Probable complete response	105 (5.4)	56 (11.8)	14 (7.6)	22 (9.2)	197 (6.9)	
Possible partial response	972 (50.1)	252 (52.9)	103 (55.7)	134 (56.3)	1,461 (51.5)	
Suspect no response	212 (10.9)	79 (16.6)	34 (18.4)	49 (20.6)	374 (13.2)	
Suspect progression	651 (33.6)	89 (18.7)	34 (18.4)	33 (13.9)	807 (28.4)	
Pre-PET treatment plan (%)						$P < 0.0001$
Continue current treatment	1,211 (62.4)	365 (76.7)	141 (76.2)	194 (81.5)	1,911 (67.3)	
Modify dose or schedule	145 (7.5)	26 (5.5)	14 (7.6)	15 (6.3)	200 (7.0)	
Switch to another treatment	571 (29.4)	81 (17.0)	28 (15.1)	25 (10.5)	705 (24.8)	
Stop treatment and switch to supportive care	13 (0.7)	4 (0.8)	2 (1.1)	4 (1.7)	23 (0.8)	
Comparison with prior bone imaging						$P < 0.0001$
Comparison made (%)	1,520 (78.4)	362 (76.1)	120 (64.9)	158 (66.4)	2,160 (76.1)	
Conventional BS (%)	423 (21.8)	71 (14.9)	11 (5.9)	25 (10.5)	530 (18.7)	
NaF PET scan (%)	1,097 (56.5)	291 (61.1)	109 (58.9)	133 (55.9)	1,630 (57.4)	
No comparison made (%)	420 (21.6)	114 (23.9)	65 (35.1)	80 (33.6)	679 (23.9)	

*Pearson χ^2 tests were used to assess association between each pre-PET profile characteristic and cancer type. If significant, certain contrasts were constructed for comparisons of interest.

[†]Abnormal tumor markers including elevated alkaline phosphatase.

For all patients combined, the pre-PET plans were to continue therapy in 67.3%, switch to another therapy in 24.8%, modify dose or therapy schedule in 7.0%, and stop systemic therapy and switch to supportive care in 0.8%. Differences were noted across cancer types. Among patients with prostate cancer, continuing current treatment was less often planned before PET (62.4% vs. 76%–82%, χ^2 $P < 0.0001$), and progressive osseous metastatic disease was suspected more often (33.6% vs. 14%–19%, χ^2 $P < 0.0001$) than for patients with other cancer types. Similarly, pre-PET plans to switch therapy were much more common in patients with prostate cancer (29.4%) than for other cancers (10%–17%,

$P < 0.0001$). For all cancer types, plans to modify dose or schedule were infrequent (7%), and plans for stopping therapy and instituting supportive care were rare (1%).

Management Changes in Light of NaF PET Findings

Table 2 shows the cross-tabulation of pre-PET plans as columns with the post-PET plans as rows by cancer type (with lung cancer combined with other cancers). Concordant pre- and post-PET plans are marked with an asterisk. The frequency of a change in plan after NaF PET (the sum of the discordances) was 40.3% overall. The frequencies of change in patients with prostate cancer

TABLE 2
Comparison of Pre-PET and Post-PET Therapeutic Plans

Post-PET plan	Pre-PET therapeutic plan				Overall change (%)
	Continue current treatment	Modify dose or schedule	Switch to another treatment	Stop treatment and switch to supportive care	
Scans (%)	1,911 (67.3)	200 (7.0)	705 (24.8)	23 (0.8)	
All cancers					40.3
Continue current therapy	1,286 (67.3)*	106 (53.0)	258 (36.6)	11 (47.8)	
Modify dose or schedule	82 (4.3)	22 (11.0)*	43 (6.1)	2 (8.7)	
Switch to another therapy	497 (26.0)	64 (32.0)	382 (54.2)*	5 (21.7)	
Stop therapy and switch to supportive care	46 (2.4)	8 (4.0)	22 (3.1)	5 (21.7)*	
Prostate cancer					41.8 [†]
Continue current therapy	790 (65.2)*	76 (52.4)	203 (35.6)	5 (38.5)	
Modify dose or schedule	46 (3.8)	16 (11.0)*	35 (6.1)	1 (7.7)	
Switch to another therapy	351 (29.0)	46 (31.7)	320 (56.0)*	4 (30.8)	
Stop therapy and switch to supportive care	24 (2.0)	7 (4.8)	13 (2.3)	3 (23.1)*	
Breast cancer					39.3 [‡]
Continue current therapy	2,534 (69.3)*	16 (61.5)	38 (46.9)	4 (100.0)	
Modify dose or schedule	17 (4.7)	1 (3.8)*	5 (6.2)	0 (0)	
Switch to another therapy	91 (24.9)	9 (34.6)	35 (43.2)*	0 (0)	
Stop therapy and switch to supportive care	4 (1.1)	0	3 (3.7)	0 (0)*	
Other cancers [§]					34.5
Continue current therapy	243 (72.5)*	14 (48.3)	17 (32.1)	2 (33.3)	
Modify dose or schedule	19 (5.7)	5 (17.2)*	3 (5.7)	1 (16.7)	
Switch to another therapy	55 (16.4)	9 (31.0)	27 (50.9)*	1 (16.7)	
Stop therapy and switch to supportive care	18 (5.4)	1 (3.4)	6 (11.3)	2 (33.3)*	

*Agreement.

[†]Difference between prostate and other cancer patients, $P = 0.018$.

[‡]Difference between breast cancer and other cancer patients, $P = 0.20$.

[§]Other cancers include lung cancer.

Rows are post-PET plans.

(41.8%) and breast cancer (39.3%) were not significantly different ($P = 0.14$), but the frequency of change was slightly lower in all other cancer types, including lung cancer (34.5%, $P = 0.006$). Initial plans for continuing therapy were changed in about one third of patients, plans of switching therapy changed in about half of patients, and less than 20% of the infrequent plans to modify dose or schedule or stop treatment were continued as the intended post-PET plan.

Comparison with Prior Scans

Prior bone radionuclide imaging was available for comparison in 76.1% of patients (bottom, Table 1). Prior NaF PET was the comparator study in 75% of those with comparators (57% of all patients), with minimal differences across the cancer types. Prior conventional BS was the comparator study in 19% of all patients, predominantly in prostate cancer patients.

Table 3 (top) shows the association between the change from prior scans, when available, and impact on post-PET plans. The findings were similar when either conventional BS or NaF PET was the comparison scan; therefore, we report only the impact when the comparison scan was NaF PET. The prior scan was obtained a median of 5.6 mo earlier (the interquartile range, 3.9–9.0 mo).

Interpreting physicians were asked to record evidence on scans of progression, and requesting physicians were asked to project prognosis based on scan results. Overall, 64% of scans showed interval nonprogression (normal, benign changes, a decrease or no change in the scan findings of metastases), whereas 36% showed progression (worsening of previously seen metastatic disease in 31% and development of new osseous metastatic disease in 5%). Among patients whose scans showed nonprogression, 79% had post-PET plans to continue current treatment versus only one third

TABLE 3
Impact of Change Since Comparison Scan and Estimated Prognosis on Post-PET Plans

Variable compared or changed	n*	Continue current treatment	Post-PET plans		Stop treatment and switch to supportive care
			Modify dose or schedule	Switch to another treatment	
All scans	2,839	1,661 (58.5)	149 (5.2)	948 (33.4)	81 (2.9)
Comparison made to prior NaF PET	1,630				
No change, normal	290 (17.8)	218 (75.2)	10 (3.4)	50 (17.2)	12 (4.1)
Resolution of previously seen metastatic disease	30 (1.8)	24 (80.0)	1 (3.3)	1 (3.3)	4 (13.3)
Decrease in metastases	275 (16.9)	238 (86.5)	10 (3.6)	22 (8.0)	5 (1.8)
No change in metastases	443 (27.2)	345 (77.9)	23 (5.2)	64 (14.4)	11 (2.5)
Progression of metastases	506 (31.0)	166 (32.8)	30 (5.9)	300 (59.3)	10 (2.0)
New metastases	86 (5.3)	30 (34.9)	5 (5.8)	50 (58.1)	1 (1.2)
Prognosis in light of PET (all scans)					
Better	796 (28.0)	643 (80.8)	37 (4.6)	74 (9.3)	42 (5.3)
No change	1,128 (39.7)	892 (79.1)	42 (3.7)	177 (15.7)	17 (1.5)
Worse	915 (32.2)	126 (13.8)	70 (7.7)	697 (76.2)	22 (2.4)

*Relative percentage of column.

of patients ($P < 0.001$) with progression. Those with progression had plans to switch to another therapy in 59%.

The referring physicians rated patient prognosis, in light of the NaF PET findings, as better in 28.0%, unchanged in 39.7%, and worse in 32.2%. Whether the prognosis was rated better or unchanged, the rates of continuing current therapy were not different (80.8% vs. 79.1%, $P = 0.36$). In contrast, when the prognosis was judged worse, current therapy was continued only 13.8% of the time (80.8% vs. 13.8% and 79.1% vs. 13.8%, both highly significant, $P < 0.001$). If the prognosis was worse, a therapy switch was planned 76.2% of the time. This was uncommon if the prognosis was better (9.3% switch) or no change (15.7% switch). The differences were highly significant (9.3% vs. 15.7% vs. 76.2%, $P < 0.001$).

DISCUSSION

The optimal type and frequency of imaging for assessing treatment response to systemic therapies in patients with metastatic cancer are uncertain; monitoring strategies in routine practice are frequently guided by those used in clinical trials (25). Generally, the same method of assessment used to detect metastatic disease at a particular site (e.g., chest CT) should be used over time to evaluate response. Standards for functional imaging techniques, in contrast to anatomic ones, are still evolving, but functional imaging is appealing because changes in metabolic indicators often precede anatomic changes (26). Assessing osseous metastasis is particularly challenging because bone lesions are generally considered to be nonmeasurable by anatomic imaging. Accordingly, functional imaging approaches may be more useful in patients with bone-dominant disease (27,28). Standards for interpreting such studies are under development; for example, new guidelines for response assessment by conventional BS in

patients with metastatic prostate cancer define progression as 2 or more new lesions on 2 subsequent treatment monitoring scans (2,29,30), and the MD Anderson Cancer Center response criteria in bone-only metastatic breast cancer do not yet include ^{18}F -FDG PET or NaF PET (27,31).

NaF PET is evolving as an important imaging method for detection of osseous metastatic disease and has both greater sensitivity and specificity than conventional BS, when imaging is performed with an integrated PET/CT scanner (11). However, NaF PET shares the same limitations as conventional BS—it is an indicator of reactive bone formation in response to various insults and is not tumor specific, and it is subject to the flare phenomenon associated with systemic therapy. Osseous changes from degenerative processes, trauma, and infection can be misleading, although these often can be diagnosed accurately based on the CT findings when the study is performed by PET/CT, as is now the dominant approach throughout the United States. The CT component of conventional BS that includes SPECT/CT provides a similar improvement in specificity, but whole-body SPECT/CT is not yet a standard procedure in general nuclear medicine practice (4).

To date, however, relatively little information is available about the impact of NaF PET on clinical decision making when used to assess the biologic response of osseous metastatic disease to guide continuing, switching, or stopping systemic therapy (28,32). Since 2011, NaF PET has been available for Medicare beneficiaries in the United States under Coverage with Evidence Development, thereby providing an opportunity to assess how NaF PET is being used in clinical practice for patients with osseous metastases.

In this report from the NOPR, we compared the management plans before and after NaF PET in patients receiving systemic therapy for metastatic cancer. In prostate and breast cancer patients, the most common plans included 2 or more types of

systemic therapy. Details about the specific drugs/products and the extent and timing of the current and preceding therapies were not collected. Four treatment-related options—continue, modify, switch, or stop all therapy—were considered. Overall, we found a 40% change in treatment plan after NaF PET.

Our current findings on the impact of NaF PET are comparable to those we have previously reported for ^{18}F -FDG PET used for treatment monitoring of chemotherapy. Those results from data collected from 2009 through 2011 were based on 15,611 patients with similar frequencies of metastatic disease but a somewhat different distribution of cancer types. Pancreas, small cell lung, and kidney cancers were most common. Only 9% had prostate cancer, and breast cancer patients were excluded because PET was covered by Medicare for treatment monitoring of breast cancer (24). Overall, therapy was changed in 48.5% of the patients in the ^{18}F -FDG PET cohort (switch, 25.9%; modify, 6.3%; and stop, 16.3%). The most notable difference was the greater frequency of stopping therapy based on the findings of ^{18}F -FDG PET.

As expected, most of the patients (79%) in whom NaF PET showed nonprogression continued on their current therapy, whereas those with evidence of progression would have a change in treatment (which occurred in 59%). From the information collected, we do not know why 41% with apparent progression continued on the same treatment, but this might have been the result of mixed responses or limited evidence of disease progression in patients with few treatment options. A worse prognosis was more likely to result in a change in treatment. In both the ^{18}F -FDG PET and the NaF PET NOPR cohorts, we assessed both disease extent and the clinical prognosis (better, unchanged, worse). ^{18}F -FDG PET resulted in a “better” prognosis rating more commonly than did NaF PET (41% vs. 28%). With both PET modalities, prognosis was rated “worse” with the same frequency (32%). Plans to continue therapy in patients with a better or unchanged prognosis were somewhat lower with ^{18}F -FDG PET than with NaF PET (66% vs. 79%). However, the impact of a “worse” prognosis on management was about the same with both ^{18}F -FDG PET and NaF PET: plans to switch therapy or to stop all therapy were the result of a “worse” prognosis (81% in the ^{18}F -FDG PET cohort and 79% with NaF PET). This may in part be a reflection of the greater uncertainty in the criteria used to define osseous metastasis response, whereas progression is usually clearer. The clinicians’ estimation of prognosis was based on their impression and not based on any defined parameters from the scan, such as lesion number, standardized uptake value, or other criteria.

Given the relatively good prognosis of bone-only metastatic disease in patients with prostate and breast cancer, prospective studies will be necessary to define the optimal interval between tests. The NOPR data do not allow us to assess whether the clinical action plans were beneficial or appropriate or whether the interval between scans is optimal. Nonetheless, our results suggest that NaF PET leads to alterations in planned treatment in a substantial fraction of patients with osseous metastatic disease. The impact of NaF PET in this setting is greatest in patients who were found to have evidence of progressive disease. Most such patients had plans of switching to a new active cancer-directed therapy rather than to supportive care.

CONCLUSION

Given the inherent limitation that this registry has a noncomparative design, we cannot claim that NaF PET is superior to traditional BS, other bone imaging approaches, or ^{18}F -FDG.

DISCLOSURE

The costs of publication of this article were defrayed in part by the payment of page charges. Therefore, and solely to indicate this fact, this article is hereby marked “advertisement” in accordance with 18 USC section 1734. NOPR is sponsored by the World Molecular Imaging Society, managed by the American College of Radiology Imaging Network, and self-supported by the fees paid by participating PET facilities. No other potential conflict of interest relevant to this article was reported.

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Bruce E. Hillner, Barry A. Siegel, Lucy Hanna, Fenghai Duan, Bruce Quinn and Anthony F. Shields

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