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Improving Reporting of Tumor Size in Synoptic Reports

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• **Context.**—Tumor size is an important prognostic feature in many synoptic reports. The best format to report this feature is not clearly defined.

Objective.—To define formatting features that impact the significance of tumor size.

Design.—We reviewed multiple formatting features of tumor size in synoptic reports and correlated them with size distribution, reproducibility, and other pathologic features.

Results.—Reporting tumors in millimeters rather than centimeters was more precise because of reduced rounding error and was significantly more reproducible ($P = .01$). Tumor sizes where the pathologist was concerned that the

size may be underestimated are associated with significantly higher tumor N stage than tumors of similar size that are not so identified. Reported tumor sizes in multifocal tumors are also associated with significantly higher N stage than unifocal tumors of the same size.

Conclusions.—Tumor sizes should be reported in millimeters, and when tumors are reported as either “at least” a specific size or as “multifocal” this information should also be recorded because these sizes likely underestimate the true biologic potential of the tumor.

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It has previously been shown that formatting can impact the pathologists’ ability to create an accurate synoptic report, a clinician’s ability to interpret that report, and can directly impact patient care.^{1–14} Tumor size is a significant prognostic feature for many tumor types in the College of American Pathologists (CAP) Microsoft Word-based and electronic Cancer Checklists.¹⁵ The best format to report this feature is not clearly defined. There are little data available concerning whether tumor sizes are best reported in millimeters, centimeters, or whether it does not matter. The most recent American Joint Commission on Cancer Staging manual is not consistent and uses both millimeters and centimeters for different tumor types.¹⁶ Recent data in melanoma suggest that there is a prognostic difference between tumors with a Breslow depth of more or less than 0.8 mm (American Joint Commission on Cancer stage T1a versus T1b).¹⁷ This suggests that the clinically relevant threshold for tumor staging (0.8 mm) may not always be at a round number (1 mm). Determining such a threshold requires accurate, precise, and reproducible measurements.

In addition, there are times when the size a pathologist reports for a tumor may underestimate the true size. This may be because the tumor is large and difficult to measure grossly (eg, invasive lobular carcinoma), it is unclear if the tumor is large, unifocal, and irregular in shape or smaller and multifocal, or the tumor extends to a margin and

appears to have been “cut through.” Typically, the size of such tumors is qualified with terms, such as “at least XX mm/cm.”

Multifocality is a required separate data element in some but not all CAP synoptic reports. Whether multifocality affects the significance of the reported tumor size has not previously been shown. To address these issues, we reviewed a large series of synoptic reports and correlated these features with the data in the report.

METHODS

We reviewed the impact of multiple formatting features on the reporting of tumor size in synoptic reports by reviewing the results in a large series of synoptic reports at our institution from 2017 to 2020 all created using a web-based system.¹⁰ In addition, to improve the statistical power of the analysis for invasive breast carcinomas 3 cm or less, additional manually created synoptic reports from 2010 to 2017 at our institution were also reviewed.

We sought to determine if the features we examined (millimeters versus centimeters, cases qualified as “at least” versus those that were not, and cases qualified as multifocal versus those that were not) affected the distribution of reported results, the reproducibility of the results, or the correlation with other pathologic features. For tumors reported in millimeters or centimeters, if the results affected the distribution of reported results this suggests a possible bias in the results. If the results were not reproducible, then this suggests that the results may not be accurate or precise. If tumors that were qualified as either “at least” or “multifocal” were associated with an increased incidence of adverse pathologic features (for example higher T or N stage) than tumors of the same or smaller size that were not so qualified, then this would be interpreted as evidence that these reported sizes are likely an underestimate of the true tumor size.

Statistical analysis was performed using a 2-tailed X^2 test or a Fishers exact test (for cases with $n < 5$) for categorical data or a Student’s t -test for continuous data. A significance level of $P = .05$ was used for all tests.

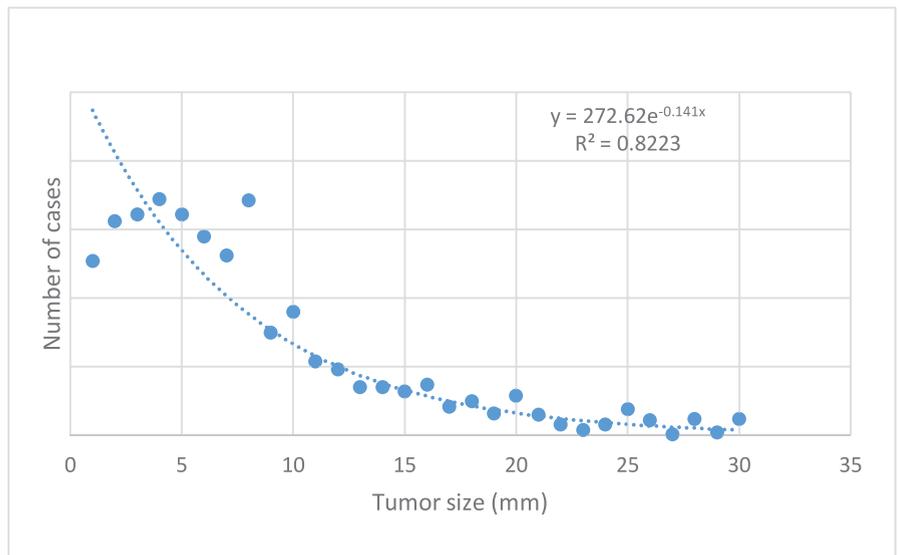
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Figure 1. Tumor sizes reported in millimeters.



RESULTS

Millimeters Versus Centimeters

We reviewed the results of 7332 synoptic reports that included tumor sizes in either millimeters (1908) or centimeters (5424). Both data sets had long tails for larger tumors, so these data were restricted to tumors 3 cm or less (1813 cases for millimeters, 3566 cases for centimeters). The distribution of the reported sizes by millimeters and centimeters are shown in Figures 1 and 2. Exponential regression showed that the data reported as millimeters have a higher R^2 correlation coefficient (0.82) than data reported in centimeters (0.08). Inspection of the figures shows that these data reported in centimeters appear to have more rounding errors (the majority of the tumors are reported as either 1.0, 1.5, 2.0, 2.5, or 3 cm). The percentage of all cases reported as these round numbers were significantly higher for cases reported in centimeters compared with those reported in millimeters (1177 of 3566 [33.0%] versus 328 of 1813 [18.1%], $P < .001$).

The pathologists could be divided into 2 distinct groups based on the hospitals of origin. The group that used

centimeters more often (63.2% versus 40.8% of cases) also has significantly more cases reported as round numbers (30.3% versus 22.5%, $P < .001$).

To verify these results, we reviewed slides and remeasured the size of the tumors from 30 consecutive cases that were reported as either 10 or 15 mm and reported in millimeters and compared them with 30 consecutive similar cases reported in centimeters. Differences of at least 2 mm in measured size occurred in 1 of 30 (3%) of cases reported in millimeters compared with 9 of 30 (30%) of cases reported in centimeters (Fishers exact test $P = .01$).

Underestimated Tumor Size

The exact phrasing that pathologists used to report tumor size in synoptic reports was reviewed, and cases where it was clear that the pathologist felt they may be underestimating the true tumor size were identified. The tumor types in which this occurred most often was invasive breast carcinoma and thyroid carcinoma. A wide variety of phrases were used, but the most common phrase was "at least XX mm/cm."

Figure 2. Tumor sizes reported in centimeters.

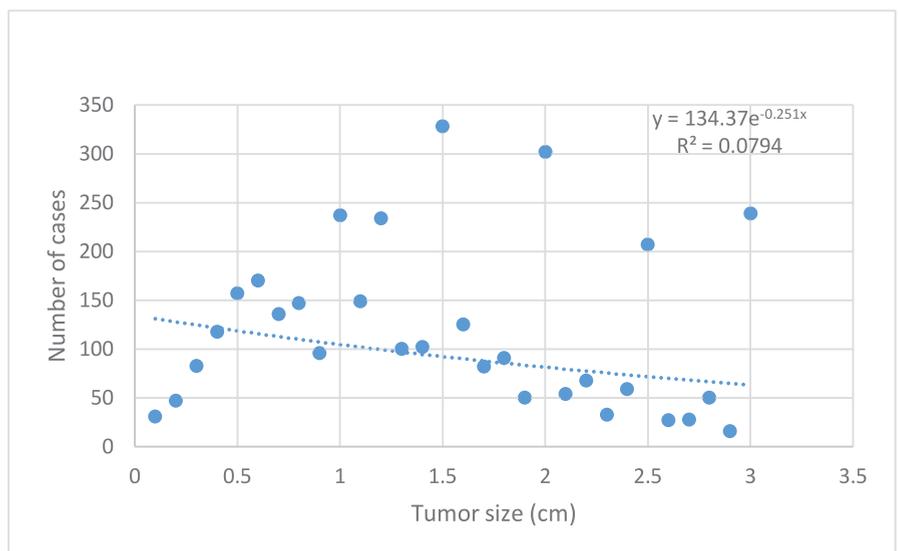


Table 1. Pathologic Features of Invasive Breast Carcinomas Whose Size is Qualified as “At Least” Versus Those That are Not			
Feature	“At Least” Cases	All Other Cases	P Value (t-test or 2-tailed X² test)
Total cases, n (%)	372 (16)	1908 (84)	
Size (mean ± SD)	19 ± 21 mm	14 ± 15 mm	<.001
Stage T3-4, n (%)	80 (21)	59 (3)	<.001
Stage N1+, n (%)	145 (48)	431 (26)	<.001
Positive margin, n (%)	121 (33)	214 (11)	.002

Lymph node resection was not available for every tumor, so the number of cases analyzed for this feature is less than the total number of cases for each group.

The data for all cases of both invasive breast and thyroid carcinomas are summarized in Tables 1 and 2. There were significant differences in tumor T stage, N stage, and margin status for both tumors when cases qualified as an underestimate (“at least” cases) were compared with those that were not. The mean size of the thyroid tumors that were qualified and those that were not qualified were not significantly different. However, the invasive breast carcinomas that were qualified were significantly larger than those that were not, suggesting that the differences may relate to the larger overall tumor size of cases that are qualified. Indeed, the majority of stage T3-4 tumors (58%) were qualified as “at least.” This suggests that pathologists have less confidence in the accuracy of their measurements as these tumors get larger.

To address this, we performed the same analysis on a consecutive series of 4000 invasive breast carcinomas 3 cm or less with lymph node dissections performed from 2010 to 2020 (Table 3). In this group the tumor sizes were not significantly different. Again, there were significant differences in tumor N stage and margin status.

Multifocality

A similar analysis was performed for multifocality on the same 4000 invasive breast carcinomas that were 3 cm or less, see Table 4. Cases that were multifocal were significantly more likely to have higher N stage and positive margin status ($P < .001$).

Table 2. Pathologic Features of Thyroid Carcinomas Whose Size is Qualified As “At Least” Versus Those That are Not			
Feature	“At Least” Cases	All Other Cases	P Value (t-test or 2-tailed X² test)
Total cases, n (%)	237 (43)	313 (57)	
Size (mean ± SD)	12 ± 16 mm	13 ± 13 mm	.42
Stage T3-4, n (%)	33 (14)	19 (6)	.003
Stage N1+, n (%)	38 (21)	20 (30)	.15
Positive margin, n (%)	67 (28)	31 (10)	<.001

Lymph node resection was not available for every tumor, so the number of cases analyzed for this feature is less than the total number of cases for each group.

Table 3. Pathologic Features of Breast Carcinomas 3 cm or Less Whose Size is Qualified as “At Least” Versus Those That are Not			
Feature	“At Least” Cases	All Other Cases	P Value (t-test or 2-tailed X² test)
Total cases, n (%)	116 (3)	3884 (97)	
Size (mean ± SD)	12 ± 7 mm	12 ± 7 mm	>.99
Stage T2, n (%)	28 (25)	913 (24)	.96
Stage N1+, n (%)	37 (32)	878 (23)	.03
Positive margin, n (%)	34 (30)	404 (10)	<.001

DISCUSSION

Our data suggest that reporting tumor sizes in millimeters rather than centimeters is more precise, more reproducible, and may be more accurate because the sizes reported in millimeters have less rounding error. This rounding error lowers the precision of the data and would make it difficult to detect a statistically significant threshold between these rounded values, such as the value previously determined for melanoma. It also has the potential to lead to a different pathologic stage if such a rounding error were near a staging threshold. However, even though we have shown the same results when our pathologists are divided into 2 different groups, we believe it is possible that the results we report for this distinction may vary from group to group. In particular, a single outlying pathologist who routinely rounds the sizes of the tumors they report may be enough to affect the results. It is also possible that if all tumors were reported in millimeters this rounding error may simply be transferred to the millimeter measurements. Additional studies may be of value to verify the best units to use to measure tumor size. Nevertheless, the reporting of tumor size in 2 different units (centimeters and millimeters) creates the possibility for a pathologist or clinician to use the wrong unit, which may affect the staging of a patient and their ultimate treatment. At the very least the consistent use of only millimeters for reporting tumor sizes eliminates this source of possible confusion and potential error.

Our data also show that pathologists are likely right when they are concerned that they have underestimated tumor size. These tumors have significantly more lymph node metastases and positive margins than tumors of similar size that the pathologist is more certain of the size they report. As a result, tumors whose sizes are qualified as possibly an underestimate should be distinguished from those whose

Table 4. Pathologic Features of Breast Carcinomas 3 cm or Less Whose Size is Listed as “Multifocal” Versus Those That are Not			
Feature	“Multifocal” Cases	All Other Cases	P Value (t-test or 2-tailed X² test)
Total cases, n (%)	251 (6)	3749 (94)	
Size (mean ± SD)	12 ± 7 mm	12 ± 7 mm	>.99
Stage T2, n (%)	40 (16)	533 (14)	.51
Stage N1+, n (%)	83 (33)	843 (22)	<.001
Positive margin, n (%)	45 (18)	406 (11)	<.001

2. Tumor size [*Millimeters preferred*]

Not applicable [*No residual tumor*]

At least

Multifocal, largest focus

Figure 3. Example of optimized formatting for reporting tumor size in synoptic reports.

sizes are not. Cases where the size of the tumor is not certain are also not directly comparable to cases where the size is certain.

At present multifocality is listed as a required data element in only a select number of CAP synoptic reports because multifocality has only been shown to affect prognosis in a selected number of tumor types. However, our data strongly suggest that multifocality has a significant impact on the meaning of the reported tumor size, a feature that is in almost all the CAP synoptic reports. As such, we believe this feature should be included in all synoptic reports to better clarify its impact on size. However, as shown in Figure 3 this does not have to be as a separate data element, but rather as an option available to the pathologist when reporting tumor size.¹⁰ This is similar to the reporting of Gleason grade/score in prostate carcinoma. These features were originally reported as separate data elements but this information was found to be more easily interpreted by clinicians when these related features were reported together in a single data element.⁸

There are limitations to this data. First, we do not have outcome data, so the result we demonstrate are limited to pathologic features. Certainly, some of the information conveyed in these qualifiers is also contained in the information included in other features, such as margin status. However, the correlation is not perfect, suggesting that the 2 features are not equivalent. For example, most pathologists recognize the difference between a positive margin where tumor has been cut across and those where the tumor appears to abut the margin. Such information may not always be conveyed in the margin assessment, but may be conveyed in a qualifier regarding size. Second, we also do not know if this information applies to tumors types other than breast and thyroid. Third, we do not believe the data we present are sufficiently powered to distinguish the impact of any individual pathologist on the results. As previously mentioned, a single outlying pathologist who routinely rounds all sizes may significantly skew the data we report on millimeters and centimeters. Fourth, there is no evidence that such an outlying pathologist would change their reporting behavior if forced to use millimeters rather than centimeters. Fifth, one recommendation to report the size of ductal carcinoma in situ in the breast is currently to count the number of blocks and then multiply by 4 mm.¹⁸ The data to support this estimate are limited primarily due to the difficulty in defining an appropriate gold standard.

While the data contained in synoptic reports may be useful in evaluating this estimate, the data we present do not directly address this issue. Finally, further more directed study of this topic may be useful to verify the results we report here.

A stated goal of the CAP is to use the data contained in synoptic reports to construct structured data sets, such as those used for tumor registries.¹⁹ These data are then used to define staging criteria, which are ultimately used to evaluate therapy. Our data suggest that tumor sizes alone are not always comparable and that the information necessary to determine which sizes are comparable is easily captured by incorporating evidence-based response options into the tumor size data element. The reporting options currently included for tumor size in the CAP protocols only include additional tumor dimensions as an optional data response. This feature has never been shown to be of any value in any tumor type. We believe there are substantial opportunities to improve synoptic reports by incorporating evidence-based formatting features. In particular all tumor sizes should be reported in millimeters, and when tumors are reported as either “at least” a specific size or as “multifocal” this information should also be recorded because these sizes likely underestimate the true biologic potential of the tumor.

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