

Melanoma Recurrence in NSW

Assessment of the feasibility of measuring melanoma recurrence in the NSW Central Cancer Registry

Final Report

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I. Introduction

Recurrence is an important outcome indicator in the treatment of melanoma. Currently there is no state wide collection of information on the recurrence of melanoma. Data on recurrence could provide melanoma clinicians with an understanding of the performance of melanoma care in NSW and the epidemiology of recurrence. It could also provide a basis for national and international benchmarking. This report contains the methods and results of a study designed to assess the feasibility of measuring the recurrence of melanoma in the NSW Central Cancer Registry (NSWCCR). The study was conducted in three distinct phases. The first was a cross-validation of known recurrences from the Sydney Melanoma Unit (SMU) with notifications to the NSWCCR. Next, a protocol was developed for measuring the recurrence of melanoma in the registry based on the findings from the cross-validation. Finally, the protocol was tested with a pilot measurement of recurrence for a random sample of 300 patients from the registry who were diagnosed with primary invasive melanoma in 2001.

II. Phase 1: Cross-validation

A cross-validation study was conducted in order to determine if known recurrences from the SMU were being reliably notified to the NSWCCR.

SMU cases

Cases were selected from the SMU Clinical Report System (CRS) database of patients diagnosed with primary invasive melanoma in 2001, had at least one recurrence by December 31, 2005, and had signed consent forms for research. Ninety-seven patients met these criteria (52% female, 48% male) and their first recurrences were distributed as follows: 28% local; 19% in-transit; 32% regional node; and 21% distant. A further 14 patients were excluded from the sample because seven were residents of the ACT, and seven were not matched in the NSWCCR. The remaining 83 patients had a total of 185 recurrences.

Nearly all of the recurrences for this study group were diagnosed with histopathology (n=169, 91%), and the remaining (n=16, 9%) were diagnosed with imaging such as X-ray, CT, or MRI.

NSWCCR notifications

The registry receives notifications of all pathology, radiotherapy, in-patient and out-patient services that either diagnose or treat cancer for NSW residents. All notifications are received and coded as episodes (type P, R, I, and O respectively) in the NSWCCR database. The episodes act as pointers to the notification documentation that is scanned and electronically archived in the Workflow Management System (WFMS). Each time a NSW resident is diagnosed with a new primary cancer, a new case is created in the NSWCCR database. Thus each patient can have a list of cases and a list of episodes that point to notifications in the WFMS.

Of the 169 histopathologically confirmed recurrences in the SMU cases, documentation in the form of pathology notifications to the NSWCCR was missing for 5 episodes (3%). The 16 recurrences diagnosed with scans were not matched with specific notifications to the NSWCCR. This was expected since diagnostic imaging, which is not a *definitive* diagnosis of melanoma, is not routinely notified to and/or coded within the registry.

Table 1. Summary of SMU recurrences not found at NSWCCR.

Type of Recurrence	Total SMU	Recurrences Dx with Scans	Histopathology not Notified to NSWCCR	
Local	39		1	3%
In-transit Metastasis	48		2	4%
Regional Node	58	3	1	2%
Distant	40	13	1	4%
Total	185	16 (9%)	5	3%

In summary, our cross-validation study revealed that the NSWCCR database alone is not sufficient to report on all recurrences. However, information in the database, specifically pathology episodes (type = P), does reliably point to electronically archived pathology reports that contain the necessary indicators for a definitive diagnosis of recurrence in 97% of histopathologically diagnosed recurrences. Therefore it is possible to measure histopathologically diagnosed recurrence of melanoma by employing a combined approach of extracting pathology episode data from the NSWCCR database, and manually reviewing archived pathology reports in the WFMS.

III. Phase 2: Measurement Protocol

Based on the cross validation study and a more detailed understanding of the NSWCCR database, we developed a protocol to identify potential histopathologically diagnosed recurrences. The measurement protocol involves three major steps; (1) select a cohort of melanoma patients of interest, (2) apply the measurement algorithm, or date test, to extract only **possible** recurrence pathology episodes from the NSWCCR database, and (3) manually retrieve and confirm the pathology reports listed as possible recurrences from the electronic archive (WFMS). The protocol is described in detail on the next page.

For the first step, it is important to select the appropriate cohort defined by date of diagnosis and possibly other characteristics such as the topography and stage of primary (Table 2).

Table 2. Possible cohorts for recurrence measurement.

Primary Melanoma Presentation	Topography Code	Stage
Primary in-situ melanoma	C44.x	A
Primary invasive melanoma	C44.x	B
Primary melanoma with advanced stage	C44.x	C,D, or E
Unknown primary site with advanced stage	C80.9	C,D, or E
Primary melanoma with insufficient information to stage	C44.x	None

Once the cohort has been selected, it is necessary to apply the measurement algorithm (date test) to select episode data for each patient that points to possible recurrence pathology in Workdesk. First, for each patient in the selected cohort, extract a list of all cases of primary melanoma (including multiple primaries), and a list of all pathology episodes (episode type =P). The measurement algorithm (see Table 3 for an example) is based on testing the date of diagnosis of each primary case of melanoma with the date of separation of each pathology episode. Where there is a match of month (MDG) and year of diagnosis (YDG), the pathology episode represents a primary pathology report and is not a possible recurrence. Also, where the second month following the month of diagnosis (MDG+1) and the year of diagnosis match, we have classified this as primary pathology. The justification for this is that wide local excisions and re-excisions of melanoma typically occur within one to three weeks following the initial biopsy. Once all primary pathology has been identified and excluded for each patient by running this date test algorithm, any episodes remaining in the list are flagged as possible recurrence pathology.

Table 3. Example of date test algorithm for one patient.

Case List	Date of Diagnosis	Topography & Stage
1	04/2001	C44.7 & Stage B
2	03/2003	C44.7 & Stage B
Episode List Pathology Only	Date of Separation	Algorithm Classification
A	15/04/2001	Primary (Same MDG/YDG as Case 1)
B	05/05/2001	Primary (Second Month/YDG as Case 1)
C	21/03/2003	Primary (Same MDG/YDG as Case 2)
D	10/10/2004	Possible Recurrence
E	04/02/2005	Possible Recurrence

After running the algorithm, generate a report that contains the identities of patients that have flagged possible recurrence pathology and the date of separation for each flagged episode. This report (see Appendix 1) represents a checklist that points to specific reports within the WFMS that must be manually sighted to determine if the episode represents a true recurrence.

The final step in the measurement protocol is to manually review all possible recurrence pathology for each patient listed on the report generated from running the algorithm. A

researcher will look up each patient in the WFMS, open each folder containing melanoma notifications, and locate each pathology report, by date of separation, corresponding to the list of possible recurrence episodes. Once each possible recurrence pathology report is located, it may be interpreted and classified as one of the following:

1. Primary pathology
2. Slide review pathology
3. Local recurrence pathology
4. In-transit metastasis pathology
5. Regional node recurrence pathology
6. Distant recurrence pathology
7. Unknown recurrence pathology (i.e. cannot distinguish between local/in-transit)
8. Missing pathology

Finally, it is necessary to count up and report on (see Appendix 2) the rate of histopathologically confirmed recurrence for the cohort selected.

IV. Phase 3: Pilot Measurement

A pilot measurement was conducted on a cohort of all patients notified to the NSWCCR with a diagnosis of primary invasive melanoma in 2001 (n=3364). From this cohort, 1502 patients had only one pathology episode in the NSWCCR database that corresponded to the date of diagnosis of the primary. As a quality assurance test, records for 20 of these patients (randomly selected) were individually reviewed in the NSWCCR database and in the WFMS to confirm they had not had a recurrence as predicted by the measurement algorithm. The overall cohort was then reduced by excluding these 1502 patients with only one pathology episode corresponding to primary pathology. A random selection of patients (n=300) was then made from the remaining 1862 patients.

The measurement protocol was trialled on the 300 patients selected at random from the 1862 patient sub-cohort described above. After running the measurement algorithm on all pathology episodes for these 300 patients, 133 patients had possible recurrence pathology, and 167 had primary pathology only. All pathology reports (n=554) were reviewed to confirm the accuracy of the algorithm. Of the 133 patients that had possible recurrence pathology, 50 had had at least one real recurrence by 2005. The summary of all pathology reports for these patients is found in Tables 4 and 5. All pathology episodes that were flagged as primary pathology by the measurement algorithm did in fact represent primary pathology reports as confirmed by the pilot measurement. The majority of pathology episodes that did not indicate recurrences but were flagged as 'possible recurrence' were actually slide reviews (n=60). The pilot measurement demonstrated that the measurement algorithm (date test) successfully picked primary pathology episodes 100% of the time, and hence real recurrence pathology episodes were reliably flagged as 'possible recurrences' for independent review and classification.

Table 4. Distribution of pathology episodes flagged as ‘Possible Recurrence’ or ‘Primary’

Possible Recurrences	Pathology Episodes	Patients
Actual Recurrences	102	50
Other	104	83
Total	206	133
Primary Pathology	348	167
TOTAL	554	300

Table 5. Reports that did not indicate recurrences but were flagged as ‘Possible Recurrence’

‘Other’ Possible Recurrence Reports	Pathology Episodes
Relating to Primary	36
Missing	4
Sentinel Lymph Node Biopsy (SLNB)	4
Review	60
TOTAL	104

As a final test of the protocol, we ran the measurement algorithm on all patients diagnosed with invasive melanoma in 2001 and extracted all case and episode data up to 2005. Application of the protocol resulted in the identification of 629 patients (19%) with possible recurrence pathology that would need to be reviewed manually by a researcher. This equates to exactly 1071 pathology reports that would need to be sighted to confirm and classify actual recurrences. Thus, our protocol reduced the number of patients for which pathology reports need to be manually reviewed from 100% of patients down to 19% of patients.

V. Discussion and Conclusions

Based on the findings of the cross-validation and the reliability of the piloted measurement protocol, we conclude it is feasible to conduct a measurement of histopathologically confirmed melanoma recurrences in the NSW Central Cancer Registry. This is possible by employing the three step measurement protocol described above. We estimate it would take a researcher approximately 6-8 weeks to conduct a review of possible recurrences for a one year cohort of patients once the data extract and measurement algorithm have been run at the NSWCCR. The result would be a recurrence measurement for a one year retrospective cohort of primary invasive melanoma patients.

The current protocol is limited to measuring histopathologically confirmed recurrences only. For example, non-resectable distant recurrences of melanoma “diagnosed” with imaging such as X-ray, CT or MRI would not be captured. We estimate from the cross-validation that these recurrences represent 9% (16 out of 185) of total recurrences. However, only two of the sixteen recurrences “diagnosed” with imaging represented a patient’s *first* recurrence, the variable most relevant to calculations of disease-free survival.

Our cross validation also suggested that almost all histopathology on recurrences are being notified to the NSWCCR. Three percent of recurrences identified in the SMU sample were not identified in the NSW CCR sample. A cross validation between the SMU and NSWCCR in one other year cohort of patients will help us to ascertain the reliability of this estimation of missing pathology in the NSWCCR.

There are two specific changes to the NSWCCR database that could reduce the workload required for future measurements of recurrence in the registry.

1. Code pathology slide reviews as a unique episode type (i.e. type = V).
2. Provide filenames for notifications in Workdesk that include the date of the episode instead of the date the notification was scanned.

First, it was observed during the pilot measurement that 30% of pathology reports that were flagged by the measurement algorithm to be a 'possible recurrence' were actually slide reviews. By coding these as a unique episode type, slide reviews could be automatically excluded by the algorithm which, in turn, would significantly reduce the amount of patients necessary for review. Secondly, if notifications were filed according to the date of the episode, possible recurrence pathology could be extracted in batches from Workdesk for review. This would also reduce the time taken to retrieve specific reports for review by the researcher conducting the measurement.

Finally, measurement of rates of recurrence through the NSWCCR may be further improved through linkage to the deaths database in such a way as to capture patients that did not have listed recurrences, but died from melanoma.

VI. Appendices

1. Data extract and date test algorithm programming summary
2. Output of proposed measurement protocol: final report

Appendix 1. Data extract and date test algorithm programming summary

- **Cohort** = All patients diagnosed with a case of melanoma in a chosen year:
 - Selection criteria
 - Morphology = 8xxx (appropriate codes for melanoma)
 - YDG = 2xxx (chosen year(s))
- **Data Extract** = All cases and pathology episodes of melanoma for each patient:
 - Case level data items
 - Morphology
 - Stage
 - Topography
 - MDG
 - YDG
 - Episode level data items
 - Episode type
 - Date of separation (format as DOS/MOS/YOS)
- **Algorithm** = Iterative test of date of diagnosis of each case with date of separation of each episode:
 - Flag primary pathology:
 - If MDG = MOS AND YDG = YOS
 - If MDG +1 = MOS AND YDG = YOS (account for rollover December – January)
 - Flag possible recurrence pathology:
 - If primary pathology tests are false for ALL combinations of cases and episodes
- **Data Output** = Spreadsheet generated for researcher to retrieve and review possible recurrence pathology reports:

Patient Full Name	Patient Date of Birth	Stage of First Case of Melanoma	Topography of First Case of Melanoma	Date of Separation of Possible Recurrence Pathology
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Appendix 2. Output of proposed measurement protocol: final report

After conducting the three step measurement protocol on all patients diagnosed with melanoma for a given year, the following is a list of the resulting reportable statistics.

1. Number of patients diagnosed with melanoma
2. Number of patients with possible recurrences of melanoma
3. Number of cases of primary melanoma per patient that are diagnosed as one of the following:
 - a. Primary in-situ melanoma
 - b. Primary invasive melanoma
 - c. Unknown primary site
 - d. Advanced stage/metastasis
 - e. Unknown stage
4. Number and date of possible recurrences, that may represent one of the following:
 - a. Real recurrences (52%)
 - i. Local
 - ii. In-transit
 - iii. Regional node
 - iv. Distant
 - v. Unknown recurrence type
 - b. Slide review report (30%)
 - c. Missing report (2%)
 - d. Relating to primary (WLE/SLNB or LN Dissection) (16%)

* Percentages extrapolated from pilot measurement (n=300)