ORAUT-OTIB-0082
Dose Reconstruction Method for Chronic Lymphocytic Leukemia

Report from the Subcommittee for Procedure Reviews (SCPR)

Presented to the

Advisory Board on Radiation and Worker Health
Oakland, California
December 11, 2019

ORAUT-OTIB-0082, "Dose Reconstruction Method for Chronic Lymphocytic Leukemia"

ORAUT-OTIB-0082 is a new document initiated to describe the use of the chronic lymphocytic leukemia (CLL) model and to provide guidance to dose reconstructors on its application.

- **Revision 00:** Issued December 04, 2012.
- **Revision 00 PC-1:** Issued December 20, 2012, to add clarification on the use of ORAUT-OTIB-0017, "Interpretation of Dosimetry Data for Assignment of Shallow Dose," and a description of the blended electron dose conversion factor to be used for assigning dose due to electrons.
- SC&A's review of Rev. 00 PC-1 was submitted October 6, 2014. SC&A was not tasked with reviewing the CLL risk model developed under contract by SENES Oak Ridge, Inc., which was used as the basis for ORAUT-OTIB-0088. The review did not identify any findings or observations. Even though there were no findings, this presentation aims to provide the Board a better understanding of the dose reconstruction methods associated with the complex CLL model.

Overview of OTIB-0082, Rev. 00 PC-1

Of all cancers assessed under EEOICPA, estimating radiation dose to cells suspected of giving rise to CLL is by far the most complex and challenging, as explained in the following statements from OTIB-0082:

- "CLL originates in the B lymphocytes rather than in a well-defined organ as with other cancers. These lymphocytes are distributed throughout the lymph system and . . . they can travel throughout the body and their inventories in various compartments of the body can change significantly with age, gender, health status and other factors" (p. 5).
- "Estimation of dose to the cancer site for CLL cases requires the calculation of the radiation dose to this population of CLL precursor cells" (p. 5).
- "In the development of the CLL dosimetric model, information was analyzed to derive compartment-specific weights based on relative sizes of B-lymphocyte . . . pools to be used in estimating a weighted average radiation dose. Because of the variability and uncertainty in the distribution of these cells, probability distribution functions were assigned to the number of lymphocytes and to the fraction that represent B cells for each organ of interest" (p. 6).

Overview of OTIB-0082, Rev. 00 PC-1 (continued)

- “The final model consists of an average dose (and its uncertainty) obtained using weights based on the fractional distribution of B-lymphocyte precursors across 30 compartments for CLL” (p. 6).
- For external dose calculation, the B lymphocytes compartments corresponding to 15 organs must be assessed (Section 4.3)
- For internal dose calculation, the B lymphocytes compartments corresponding to a total of 28 organs must be assessed (Section 4.2).
- For medical x-ray dose calculation, the B lymphocytes compartments correspond to 18 organs (Section 4.1).
- The corresponding ICRP-modeled organs to be assessed for each compartment of the CLL model are shown in OTIB-0082, Table 3-1 (reproduced here in Slide 5).

Correspondence of CLL model to ICRP-modeled organs (OTIB-0082, Table 3-1)

Compartment of CLL dosimetry model	X-ray dose organ	Internal dose organ	External dose organ
Lymph nodes			
Extrathoracic	Thyroid	LN(ET)	Thyroid
Thoracic	Lung	LN(TH)	Lung
Remainder	Ovaries	HNM	Stomach
Spleen	Spleen (lung or ovaries)	Spleen	Stomach
Peyer's Patches	Colon (ovaries)	SI	Stomach
Thymus	Thymus (lung)	Thymus	Thymus
Red bone marrow	Bone marrow	RBM	RBM
Tonsils	Esophagus (lung)	LN(ET)	Esophagus
Blood	Remainder	HNM	Stomach
Intestinal mucosa			
Small intestinal wall	Ovary	SI	Stomach
Upper intestinal wall	Colon (ovaries)	ULI	Colon
Lower large intestinal wall	Colon (ovaries)	LLI	Colon
Respiratory mucosa			
Extrathoracic airways	Esophagus (lung)	ET2	Esophagus
Lung	Lung	Lung	Lung
Skin	Skin	Skin	Skin
Liver	Liver (lung or ovary)	Liver	Liver
Vermiform appendix	Colon (Ovaries)	ULI	Colon
Residual soft tissue			
Muscle	Remainder	Muscle	Remainder
Breast	Breast	Breast	Breast
Kidneys	Remainder	Kidney	Liver
ST wall	Stomach (lung or ovaries)	Stomach	Stomach
Pancreas	Pancreas (lung or ovaries)	Pancreas	Stomach
Uterus	Uterus	Uterus	Uterus
Urinary bladder wall	Urinary bladder (ovaries)	Bladder	Bladder
Esophagus	Esophagus (lung)	Esophagus	Esophagus
Testes	Testes	Testes	Testes
Thyroid	Thyroid	Thyroid	Thyroid
Prostate	Prostate (ovaries)	HNM	Bladder
Adrenals	Remainder	Adrenals	Remainder
Ovaries	Ovaries	Ovaries	Ovaries

External Dose

- To account for the correlation of external dose between dosimeter measurements and the individual organs listed in OTIB-0082, Table 3-1, a special dose conversion factor (DCF) was derived and is used to determine the dose to the appropriate CLL compartments.
- This blended CLL DCF, which is described in DCAS-RPT-004, “Chronic Lymphocytic Leukemia (CLL) Dose Conversion Factors,” is composed of the weighted fractions of the DCF values associated with the 15 organs listed in Table 3-1.
- Blended DCFs are based on previously assessed DCF values cited in OCAS-IG-001, “External Dose Reconstruction Implementation Guide,” for selected radiation types, energies, and exposure geometries using Monte Carlo techniques.

External Dose (continued)

- For each CLL DCF, NIOSH employed a total of 50,000 iterations, which were fitted to five standard probability distributions that included normal, lognormal-3 parameter, lognormal-2 parameter, Weibull-3 parameter, and Weibull-2 parameter.
- NIOSH determined the best fit of the data among the five distributions using the Akaike Information Criterion (AIC) and selected the fit(s) with the lowest AIC score.
- To properly apply the blended DCF values in dose reconstruction, NIOSH added a "CLL DCF" tab/spreadsheet with these CLL DCFs to all site-specific external dose calculation workbooks.
- SC&A's review:
  - Critically reviewed the statistical approach described in DCAS-RPT-004.
  - Verified that the site-specific external dose calculation workbooks had been updated with the "CLL DCF" tab, and that the data entered into the spreadsheet associated with this tab were consistent with data given in DCAS-RPT-004.
- SC&A concurred with the methodology used to derive blended CLL DCF values.

Internal Dose

- Given the complexity of deriving weighted organ/tissue doses, NIOSH developed the CLL Simulator Tool, which allows the Integrated Modules for Bioassay Analysis (IMBA) and Chronic Annual Dose Workbook (CADW) files to be imported for calculating internal doses to all CLL organs simultaneously.
- The CADW was also modified to create a separate file for each of the 28 organs/tissues, which can be used in the CLL Simulator Tool.

Internal Dose (continued)

- CLL-specific guidance was added to the following list of applicable documents to address the complexity of the CLL risk model:
  - ORAUT-OTIB-0018, “Internal Dose Overestimates for Facilities with Air Sampling Programs”
  - ORAUT-OTIB-0054, “Fission and Activation Product Assignment for Internal Dose-Related Gross Beta and Gross Gamma Analyses”
  - ORAUT-OTIB-0049, “Estimating Doses for Plutonium Strongly Retained in the Lung”
  - ORAUT-OTIB-0011, “Technical Information Bulletin: Tritium Calculated and Missed Dose Estimates”
  - Site-specific radionuclide chooser tools
  - Site-specific internal environmental tools

Internal Dose (continued)

- SC&A was provided training on running the CLL Simulator Tool. Subsequently, SC&A generated both IMBA and CADW files for a CLL claim, imported these files into the CLL Simulator Tool, and evaluated the internal doses generated by the tool.
- SC&A assessed the changes made to tools and to dose reconstruction guidance for performing internal dose estimates.
- SC&A's evaluation of internal dose tools confirmed that appropriate changes have been incorporated into these tools, and that the tools generated internal doses that included the weighted organs/tissues specified in OTIB-0082.
- SC&A's evaluation of the technical guidance verified that appropriate changes were incorporated for performing best estimates for CLL claims.

Medical X-ray Dose

- For occupational medical radiation associated with either a chest or lumbar spine x-ray examination, dose estimates to each CLL compartment are defined by the product of the incident air kerma and the compartment-specific DCFs assigned to organs shown in the second column of Table 3-1.
- For the CLL compartment involving the skin, an entrance and exit skin dose is defined, as well as the fraction of exposed skin, which varies from 0.19 for a properly collimated beam to 0.38 for a poorly collimated beam.
- The effective organ dose to CLL precursor cells from occupational medical exposure is the sum of the weighted organ doses that takes into consideration uncertainties associated with each organ-specific DCF value and the weighted fraction of CLL cells.

Medical X-ray Dose (continued)

- For estimates of CLL medical x-ray doses, NIOSH developed CLL x-ray doses that were facility specific, view specific (e.g., PA or LAT), and facility specific to given time periods.
- Variables among time periods included assigned organ doses and whether beams were properly or poorly collimated.
- A lookup table containing these values has been incorporated into each site-specific external dose calculation workbook as a single tab (“CLL X-ray Data”).

Medical X-ray Dose (continued)

- SC&A's review consisted of:
  - Evaluating NIOSH's methodology and guidance pertaining to the assignment of medical x-ray dose to compartments. These indicated that they are consistent with existing models and, when properly adjusted to account for the distribution of CLL precursor cells among compartments, comply with the CLL risk model.
  - Examining all site-specific external dose calculation workbooks to ensure that the 'CLL X-ray Data" tab had been added and the data were consistent with technical basis document guidance.

Validation of Guidance in ORAUT-OTIB-0082 by Dose Reconstruction

- To assess the functionality of the guidance in OTIB-0082, SC&A conducted a preliminary review of a CLL case assigned as part of our audit of the 19th set of dose reconstructions.
- The CLL case review included evaluation of (1) photon/neutron doses, (2) occupational medical exposure, (3) bioassay data, (4) IMBA inputs and results, and (5) the CLL Simulator Tool.
- From this preliminary evaluation and a spot check of calculations, doses, etc., it appears that, for this case, the dose reconstructor used the proper procedures and assigned the correct doses.

Questions?