Genetics Working Group

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Genetics WG Resources

- Syndromic phenotype:
  - Congenital anomalies
  - Cancer family history
- Constitutional DNA for genotyping
- Tumor-specific tissue for genotyping, profiling, methylation studies

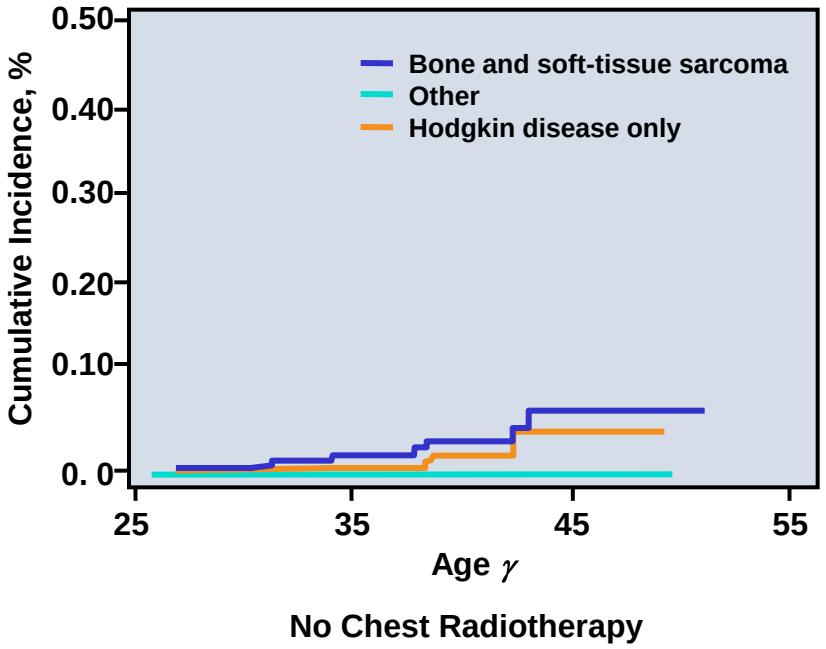
Publications

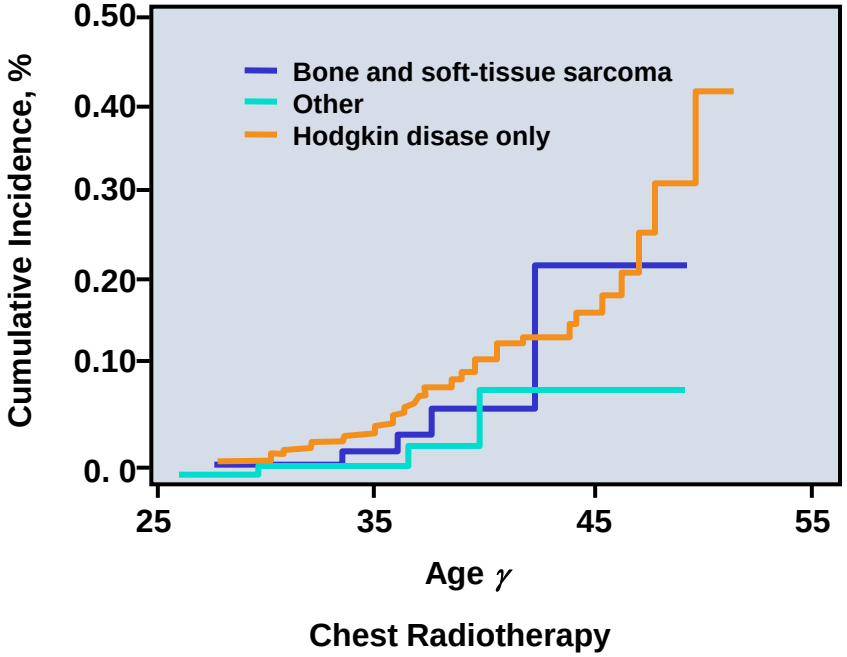
- Kadan-Lottick et al, 2003
  - Clarification of cancer family history
- Friedman et al, 2005
  - Cancer in siblings of LTS

Cancer FH in collaboration with SMN WG:

- Henderson et al, 2007
  - Secondary sarcomas…

Cumulative Incidence of Breast Cancer in Childhood Cancer Survivors by Attained Age and XRT





Kenney et al, 2004 for the Childhood Cancer Survivor Study

CCSS: Association of SMN in Proband and Cancer Risk in Sibling

Proband:	SMN	No SMN	
Sibling SIR	2.4	1.4	P<0.05

30% of siblings had same cancer as first or second proband cancer

Friedman et al, 2005

Ongoing Genetics WG Activities

- Single gene syndromes in LTS –
  - Mulvihill et al
- HL Genome-wide association study –
  - J Bernstein et al
- Family history questionnaire –
  - web based or interview, probes
- Risk modifiers for SMN
  - MDM2 SNP309 in HL/breast (Davies, Strong)

Genetics WG: Resources for Gaps, Future Opportunities

Evaluate genetic contribution to initial childhood cancer, multiple primary tumors and other LE

- Biospecimen repository up front for new cohort to include probands and parents, new samples on existing cohort
- New focused web-based family history questionnaire for existing and expanded cohorts
- Offspring cohort, biospecimens not dependent on proband survival
- Genetic predisposition to complement the outstanding repository of data on childhood cancer, treatment and late effects

Genetics WG: Priorities, Potential RFAs

- Tumor-specific genetic changes, dependent on tumor/normal resources
  - Tissue or histology specific?
  - Treatment specific?
  - Genetic predisposition-specific?
- Genetic testing/counseling in LTS & fams
- Ethics and genetic testing in CCSS
- “Biomarkers” of increased SMN genetic risk
- Significance of change in cancer family history over time