# Incidence Of Primary Brain And Other Solid Tumors Following Low And High Dose Radioactive Iodine Therapy In Hyperthyroidism And Thyroid Cancer. Is It Coincidence Or Is There A Real Association?

John Hollis Tackett[1], Johnny Yang[1], Marjorie Lam[1], Easton Sheffield[1], Chanukya Cherukuri[1], Bryson Brister[1], John D. Salvemini[1], Vani Vijayakumar MD[2]

[1]School of Medicine, UMMC; [2]Department of Radiology, UMMC

## INTRODUCTION

**Teaching Points:**

- To review the use of low-dose & high-dose radioactive iodine (RAI) therapy in the treatment of hyperthyroidism and differentiated thyroid cancer (DTC)
- To evaluate the risk of subsequent tumor development (specifically primary brain tumors or other solid tumors) after receiving RAI therapy for hyperthyroidism or DTC
- To compare findings from relevant literature to case examples from a tertiary academic center

**RAI Therapy:**

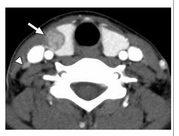
- Use of radioisotope I-131 to permanently destroy thyroid tissue via β- radiation
- Can be administered orally or intravenously

**Low-Dose RAI Therapy:**

- Dosage range: 148-370 MBq
- Most commonly used to treat Graves' hyperthyroidism, toxic adenoma, & toxic multinodular goiter after initial medical treatment
- Indicated for patients who are:
  - Over age 21
  - Not pregnant/planning on getting pregnant within a year after treatment
  - Poor surgical candidates
  - Contraindicated for thioamides

**High-Dose RAI Therapy:**

- Dosage range: 3700-5550 MBq
- Most commonly used to treat well-differentiated thyroid cancers (like papillary thyroid cancer)
- Indicated for patients post-thyroidectomy to:
  - Destroy remaining normal thyroid tissue
  - Lower recurrence risk in moderate-to-high risk patients
  - Destroy cancer remaining post-surgery
  - Destroy any present metastatic cancer



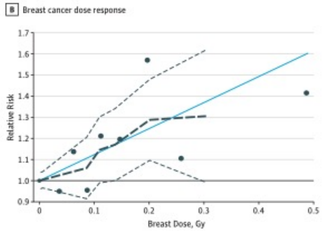
## METHODS

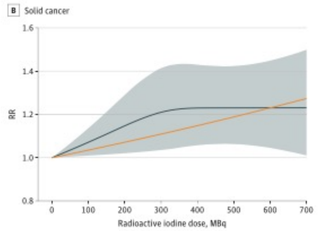
- Databases Medical Literature Analysis and Retrieval System Online (MEDLINE)/PubMed and Google Scholar were used for the literature search between 2013 and 2023.
- Key words: "radioactive iodine treatment," "cancer risk," "cancer mortality," "hyperthyroidism," and "DTC."
- Editorial, commentaries, and unpublished works were excluded.

## RESULTS

**Risks for Treatment of Hyperthyroidism:**

- Kitahara C et al.
- N = 18,805
- Significant positive association observed for all solid cancer mortality (RR = 1.06)
- Risk for breast cancer mortality especially elevated (RR = 1.12)
- Risk still elevated for all other solid cancers combined besides breast cancer (RR = 1.05)

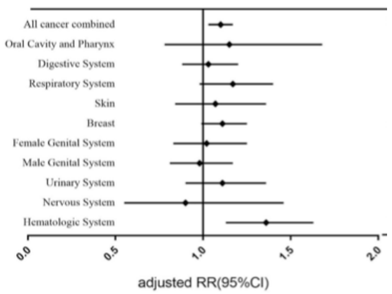



- Shim S et al.
- N = 479,452
- Overall risk for cancer incidence not statistically significant (RR = 0.91)
- Significant linear dose-response positively associated between RAI therapy & solid-cancer mortality (RR = 1.14), especially breast cancer (RR = 1.35)

**Risks for Treatment of DTC:**

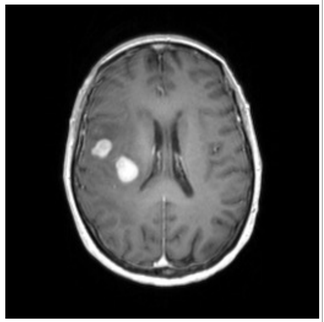
- Mei X et al.
- N = 104,026
- Slight elevation in risk for subsequent development of all combined malignancies (RR = 1.10)
- Elevated risk of breast malignancy development (RR = 1.14)
- Unclear risk shown for neurologic malignancies (RR = 0.98; 95% CI = 0.58-1.65)




- Risk of developing malignancy elevated in first 5 years post-DTC diagnosis (RR = 1.11) but gradually decreased as time passed
- Attribution of RAI therapy to all cancer combined subsequent malignancies estimated to be only 0.9%
- Tumor features and mortality were similar between patients treated with RAI therapy and those who were not

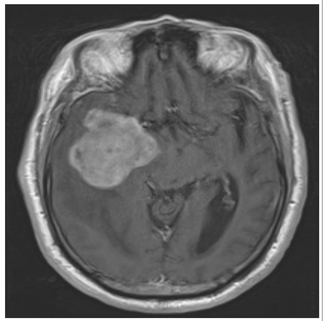
**Case 1: Brain Tumor in Grave's Disease Patient:**

- 73 y/o Caucasian female
- Treated for Grave's Disease with RAI therapy at unknown date before admission
- Presented to outside hospital with left hemiparaplegia & unsteady gait in 2020
- Two parietal lesions observed on MRI
- Diagnosed with glioblastoma upon pathologic examination of biopsy:
  - WHO grade IV
  - IDH ½ wild type
  - ATRX intact
  - BRAFV600E negative
- Treated with chemo



**Case 2: Brain Tumor in DTC Patient:**

- 67 y/o African American male
- Diagnosed with DTC in 2005
- Treated with RAI therapy & thyroidectomy in 2006
- Presented to ED with left-sided weakness, headache, & partial seizures in 2020
- Mass observed on MRI
- Diagnosed with gliosarcoma upon pathologic examination of biopsy:
  - WHO grade IV
  - IDH1 R132H negative
  - ATRX intact
- Tumor removed in 2020
- Underwent chemo, novoTTF, C1, and C6 the year following removal
- Recurrence of glioblastoma in 2023
- Deceased



## CONCLUSION

**Key Take-Away Points:**

- Higher & multiple doses in younger patients poses risk for future malignancy development due to long latent period
- Cancer development in older patients most likely a coincidence and instead associated more with aging

**For Treatment of Patients with Hyperthyroidism:**

- Patients at risk for breast cancer should be closely monitored when administering RAI therapy
- Caution should be taken when using higher RAI doses due to increasing mortality risk with increasing dose

**For Treatment of Patients with DTC:**

- Despite increased risk for development of solid cancer, absolute number of cases would most likely be low due to low incidence in thyroid cancer survivors
- Patients are most at risk of subsequent malignancy development in first 5 years after diagnosis of DTC
- More research needed to further investigate potential association between RAI therapy and development of neurologic malignancies

**Comparison of Presented Cases to Literature Findings:**

- No evidence found of significant positive association between RAI therapy and subsequent neurological malignancy development
- Hard to determine the risk associated with the patient in Case 1 due to the lack of knowledge on how long it had been since they had undergone RAI therapy
- Most likely that tumor present in the patient in Case 2 not associated with RAI therapy exposure
  - Tumor discovered 14 years after exposure to RAI; RR observed by Mei et al. for latency time of 10-15 years for all combined cancer was 0.88

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## AUTHOR CONTACT INFORMATION


- John Hollis Tackett: jtackett1@umc.edu
- Vani Vijayakumar: vvijayakumar@umc.edu