Supplementary Online Content

Baumann BC, Verginadis II, Zeng C, et al. Assessing the validity of clinician advice that patients avoid use of topical agents before daily radiotherapy treatments. *JAMA Oncol*. Published online October 18, 2018. doi:10.1001/jamaoncol.2018.4292

This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods 1. Dosimetric and Preclinical Radiation Technique and Staining

Preclinical radiation technique

Mice were focally irradiated (320kV, 12.5mA, 50cm SSD, 0.85Gy/min with Al/Cu/Sn filtration) using the XRAD 320ix X-ray animal irradiator (Precision X-ray, North Branford, CT) with lead shielding to protect the head and distal hindquarters. Calibration of the device was performed using the TG61 protocol.[1]

γ-H2AX immunofluorescence

Five-to-seven micrometer-thick cross sections of the skin were used for immunodetection of various proteins and markers. OCT embedded samples were analyzed for DNA double strand breaks using a procedure modified from a method reported by Tang *et al.*[2] Sections were fixed with 2% (w/v) paraformaldehyde (PFA) in phosphate-buffered saline (PBS) for twenty minutes. Sections were washed twice in PBS for fifteen minutes each, treated with 70% ethanol at -20°C, before being washed three more times in PBS for ten minutes each. Next sections were blocked in 8% bovine serum albumin (BSA) in PBS containing 0.5% Tween-20 and 0.1% Triton X-100 (PBS-TT) for one hour at room temperature in a humidified staining trough. Sections were washed with PBS-TT for five minutes before the buffer was tipped off. Then 100 microliters of the directly FITC conjugated anti-phospho-Histone H2AX (Ser139) antibody (Millipore, clone JBW301, 16-202A, Billerica, MA) diluted 1:500 in 1% BSA in PBS-TT were added to each section. Slides were then incubated for two hours at room temperature in a humidified staining trough. Sections were washed three times with PBS-TT for five minutes each then counterstained with 100 microliters of 5µg/ml of Hoechst (Molecular Probes, 33342, Eugene, OR) for 30 minutes, washed in PBS-TT, and mounted in Vectashield medium (Vector Laboratories H-1000, Burlingame, CA).

TUNEL immunofluorescence

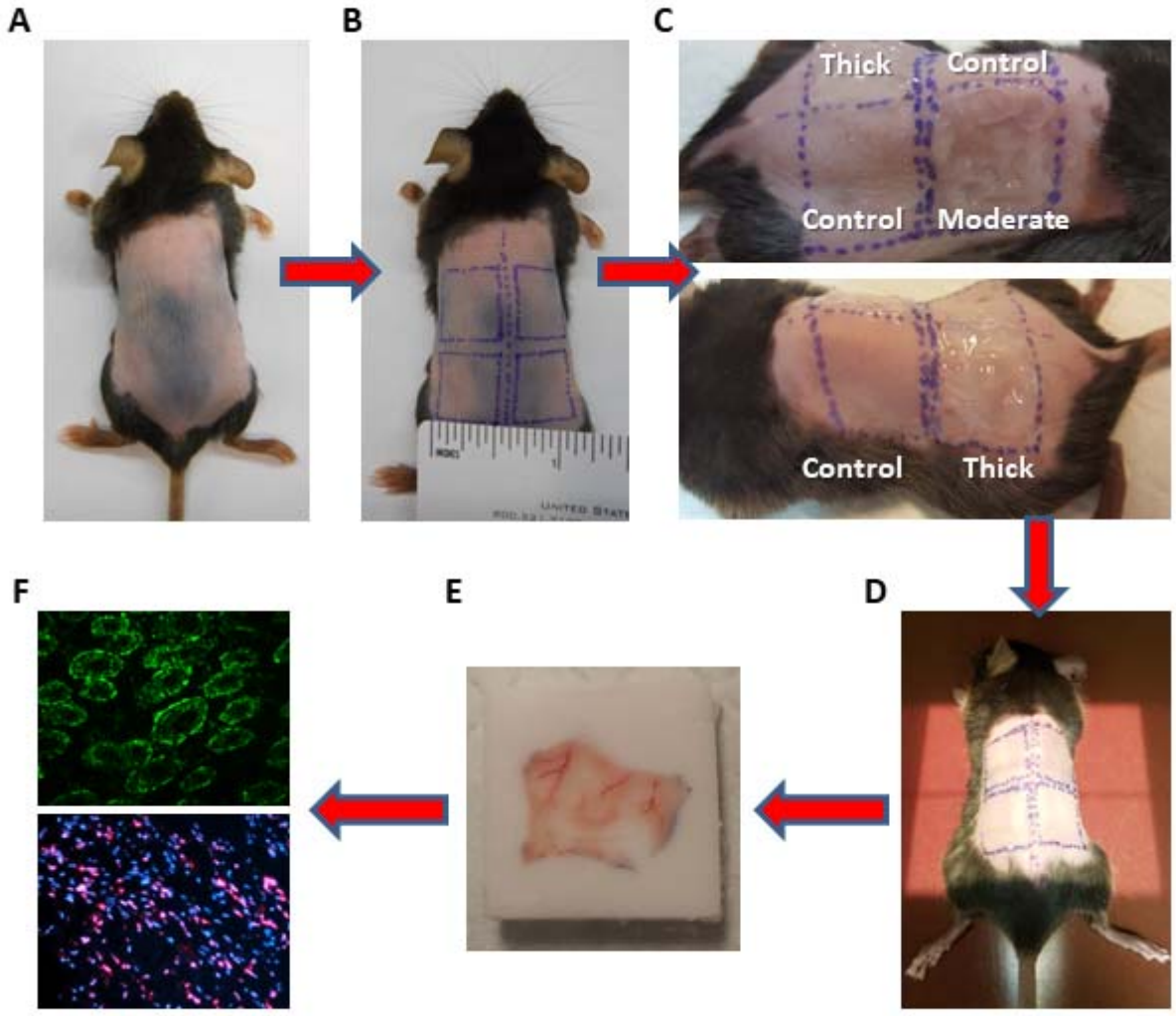
Apoptosis was detected with the *In Situ* Cell Death Detection Kit, Fluorescein (Roche 11684795910, Pleasanton, CA) using the TdT mediated dUTP nick end labeling (TUNEL) method. OCT embedded tissue sections were fixed in 4% (w/v) PFA for twenty minutes at room temperature then washed in PBS for thirty minutes. Next, sections were incubated in 0.1% Triton X-100, 0.1% Sodium Citrate in PBS on ice. The TUNEL reaction mixture was then prepared according to the manufacturer's instructions. Slides were rinsed twice in PBS then incubated in the TUNEL reaction mixture in a humidified staining trough for one hour at 37°C. Slides were washed with PBS and incubated with Hoechst for thirty minutes, washed in PBS, then mounted in Vectashield medium.[3]

Statistical Analysis

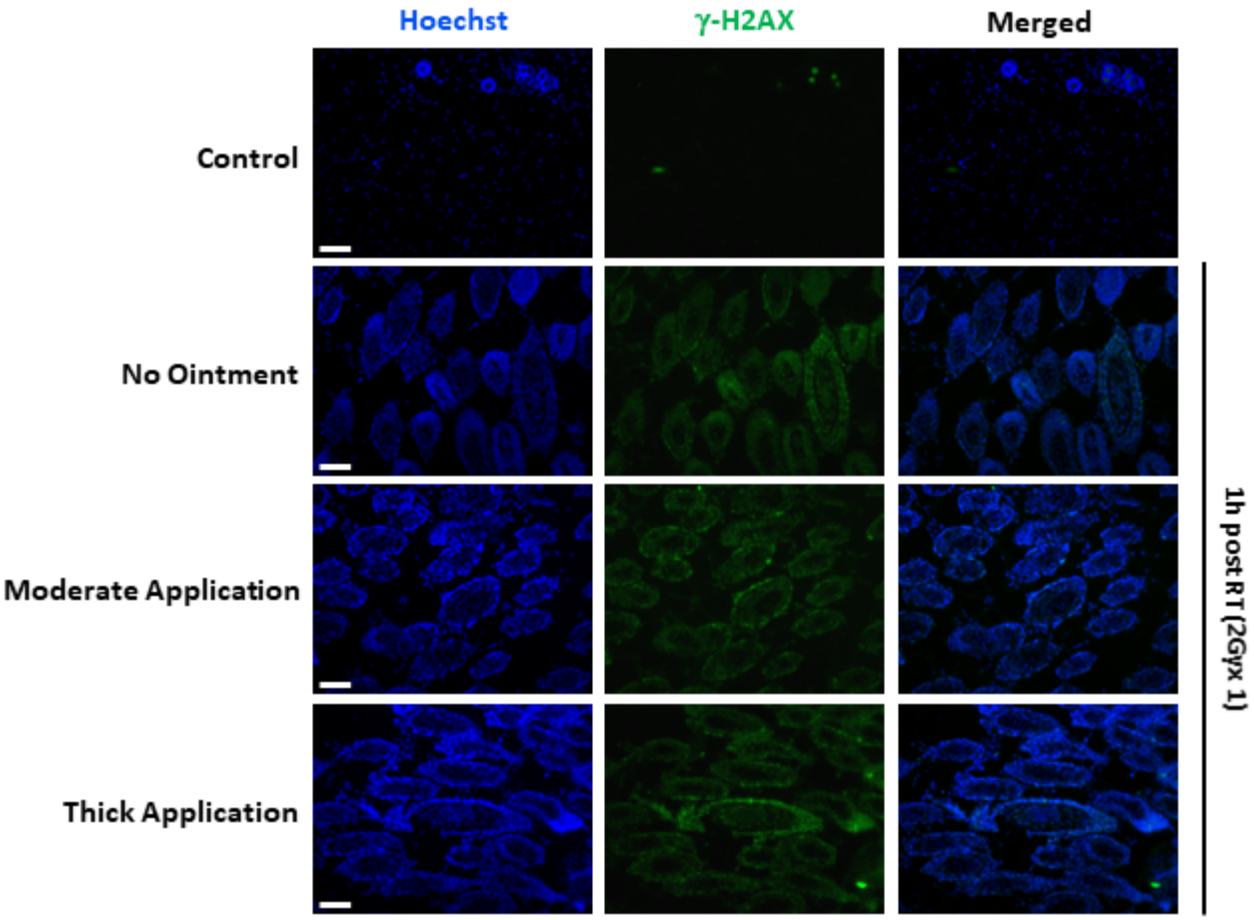
GraphPad Prism VI was used to analyze preclinical data. Ordinary one-way ANOVA with Tukey's multiple comparisons test was used to determine statistical significance. The alpha value was set at 0.05. Data presented as mean ± SEM (n=3).

SUPPLEMENTAL FIGURES

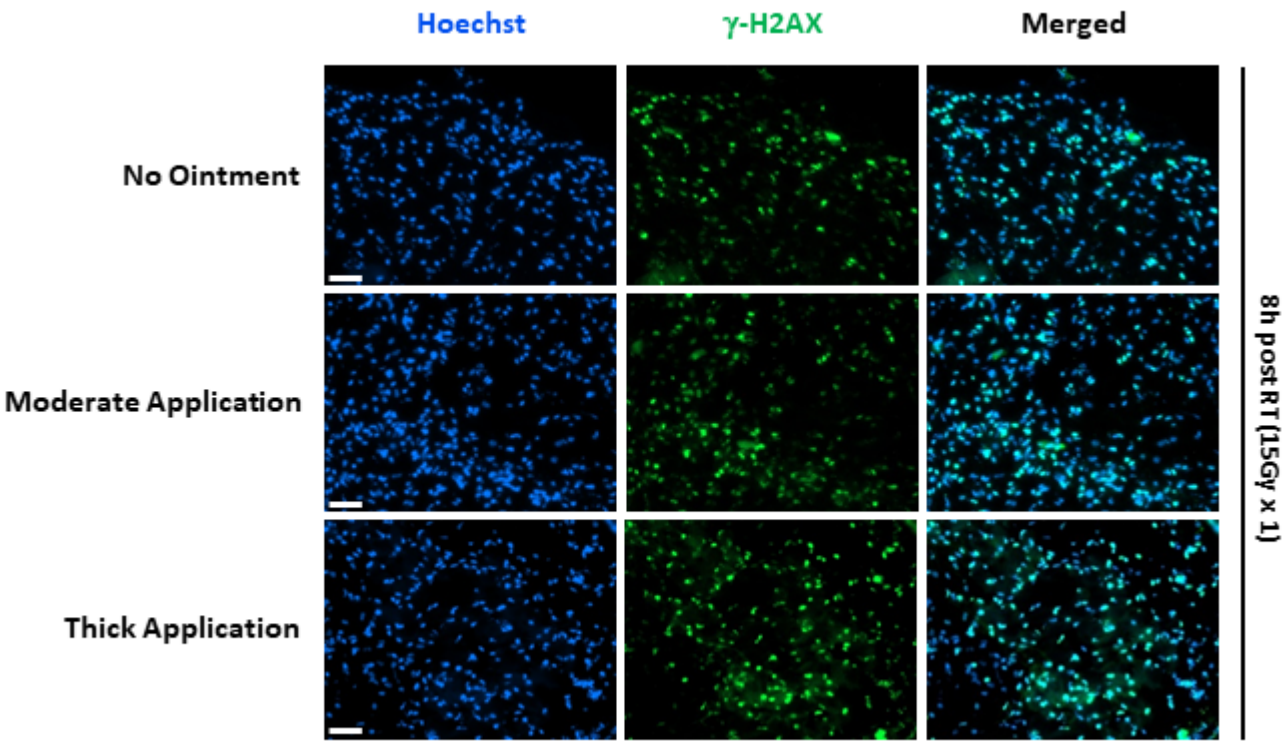
eImage. Dosimetric experimental setup



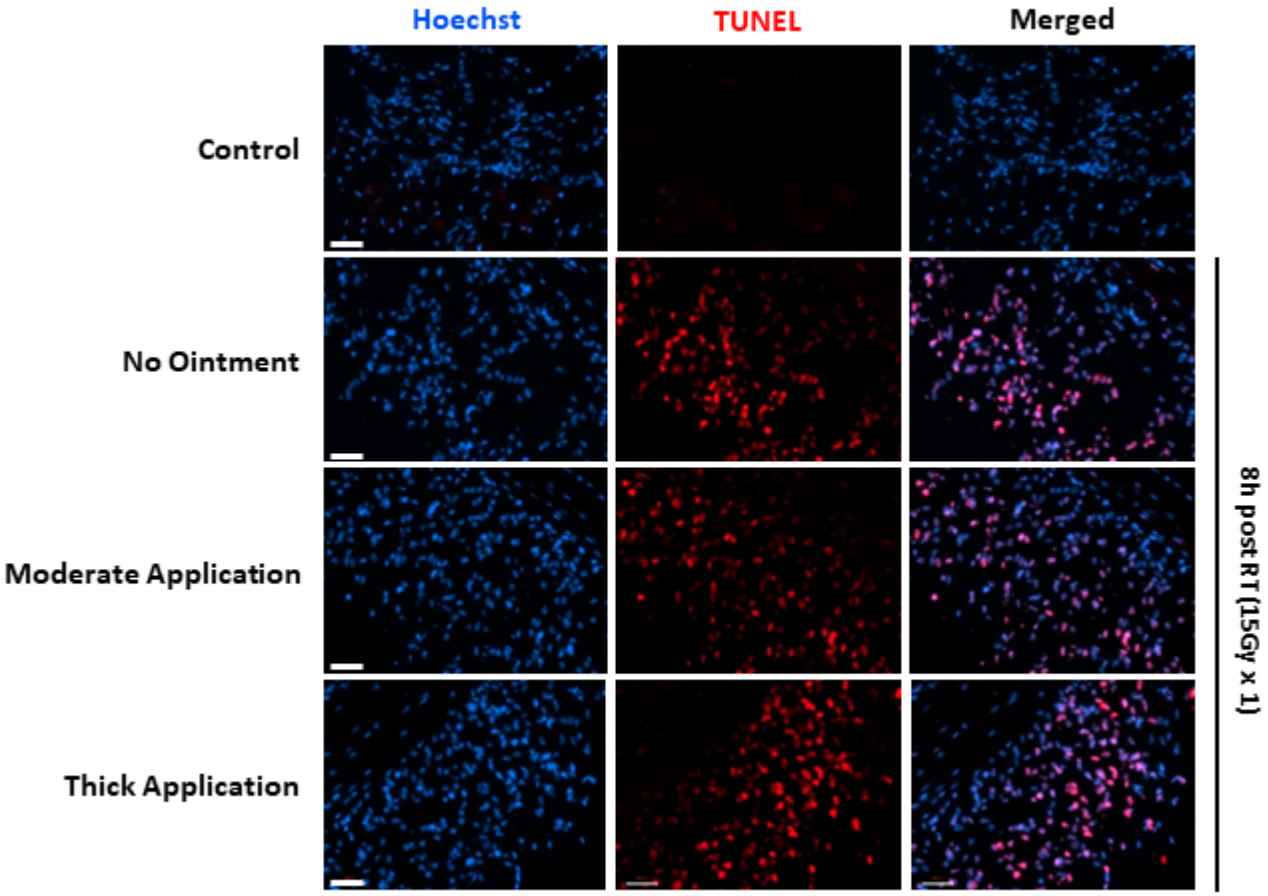
eFigure 1: Schematic Presentation of the Experimental Design. **A)** Hair removal, **B)** Drawing a 2x2 square grid (0.5x0.5" each), **C)** Application of 50mg of petroleum-based ointment (Aquaphor, petrolatum 41%) on the upper right square (moderately thick application – Moderate) and 200mg on the lower left square (thick application – Thick) (other 2 squares were used as internal controls), **D)** Irradiation of the marked areas with 2 Gy ×1 or 15Gy ×1 using XRAD 320ix X-ray animal irradiator, **E)** Harvested skin tissues placed in OCT molds 1h post RT, **F)** Cut sections stained for γ-H2AX (upper) or TUNEL (lower) staining.



eFigure 2: γ-H2AX Staining in Frozen Sections of Skin From Control Mice (Untreated) Compared With Skin Sections from Mice Irradiated to 2 Gy ×1 +/- Application of Petroleum-based Ointment of Varying Thickness, at 1 hour post RT. Representative images from Control (no RT), irradiated tissue with 2Gy (no ointment), application of 50 mg of ointment (Moderate Application) and RT with 2Gy; and application of 200mg of ointment and RT with 2 Gy (Thick Application). Nuclei are counterstained with Hoechst (blue) containing γ-H2AX foci (green); 10x magnification; scale bar 50μm.



eFigure 3: γ-H2AX Staining in Frozen Sections of Skin From Mice Irradiated to 15Gy ×1 in the Presence or Absence of Petroleum-based Ointment of Varying Thickness, Including Application of 50mg (Moderate Application) and Application of 200mg (Thick Application). Nuclei are counterstained with Hoechst (blue) containing γ-H2AX foci (green); 10x magnification; scale bar 50μm.



eFigure 4: TUNEL Staining in Frozen Sections of Skin from Control Mice Compared with Skin Sections from Mice Irradiated to 15Gy ×1 in the Presence or Absence of Petroleum-based Ointment of Varying Thickness. Representative images from control (no RT), tissue irradiated to 15Gy in the absence of ointment (No Ointment) or in the presence of 50mg of petroleum-based ointment (Moderate Application) and 200mg of petroleum-based ointment (Thick Application) are shown. Nuclei are counterstained with Hoechst (blue) containing TUNEL positive cells (red); 10x magnification; scale bar 50µm.

eReferences

1. Ma CM, Coffey CW, DeWerd LA, et al. AAPM protocol for 40-300 kV x-ray beam dosimetry in radiotherapy and radiobiology. *Medical physics.* 2001;28(6):868-893.
2. Tang MM, Mah LJ, Vasireddy RS, et al. Quantitation of gammaH2AX foci in tissue samples. *J Vis Exp.* 2010(40).
3. Verginadis, II, Kanade R, Bell B, Koduri S, Ben-Josef E, Koumenis C. A Novel Mouse Model to Study Image-Guided, Radiation-Induced Intestinal Injury and Preclinical Screening of Radioprotectors. *Cancer research.* 2017;77(4):908-917.

eMethods 2. Patient and Provider Survey Forms

Skin cream usage for radiation-related skin reactions: An internet-based patient survey

This information is part of a process called “informed consent” to allow you to understand this study before deciding whether to take part.

The following survey will help us to understand skin cream usage by patients who develop skin redness/irritation during radiation therapy.

This anonymous online survey contains a total of 24 multiple choice questions. There is no time limit, though some people take about 10 minutes to complete the survey.

We will collect some basic information from you such as age, sex, education, and the like. The information collected in this survey is confidential and the researchers will NOT be able to identify who is filling out the information. In the report of this study, you will not be recognizable and all personal health information will be protected.

Only the investigator for the study and the study team may use or share your information, and we will not disclose the information outside of the University of Pennsylvania Health System (UPHS).

This survey is for adults, 18 years of age or older, who previously had a diagnosis of cancer and who were treated with radiation therapy. Your participation in this study is voluntary.

The benefits for taking part in this study include generating information to better help health professionals provide the best care to cancer patients. You may receive no benefit from your participation. There will be no compensation for you or your time spent on this survey.

Contacts and Questions

Principal Investigator: James Metz, MD

Co-investigator: Brian Baumann, MD

All questions or other comments may be sent to Brian Baumann at the following:

Email: Brian.Baumann@uphs.upenn.edu (mailto:Brian.Baumann@uphs.upenn.edu)
Phone Number: 215-662-2428

If you have questions about your rights as a research subject you may contact the Office of Regulatory Affairs at 215-898-2614.

Statement of Consent

Completion of the following survey indicates my consent to participate.

* Required

Statement of Consent *

Completion of the following survey indicates my consent to participate.

☐ I have read the above information and I feel I understand the study well enough to make a decision about my involvement.

Please indicate your gender: *

○ Male

○ Female

○ Prefer Not to Answer

Please indicate you current age: *

Under 18 ▾

Please indicate your racial background:

☐ African American

☐ Asian/Pacific Islander

☐ Caucasian

☐ Latino/Hispanic

- [ ] Mixed Race
- [ ] Other

Please indicate the highest level of education completed: *

- ( ) Less than 8th grade
- ( ) 8th – 11th grade
- ( ) High school diploma
- ( ) Some college
- ( ) College degree
- ( ) Graduate school (masters degree, PhD, MD, JD)

Please indicate the type of cancer diagnosed? (Please select all that apply.) *

- [ ] Acute Lymphocytic Leukemia
- [ ] Acute Myeloid Leukemia
- [ ] Anal Cancer
- [ ] Appendiceal Cancer
- [ ] Bladder Cancer
- [ ] Brain Cancer
- [ ] Breast Cancer
- [ ] Cervical Cancer
- [ ] Chronic Lymphocytic Leukemia
- [ ] Chronic Myelogenous Leukemia
- [ ] Colon Cancer
- [ ] Endometrial Cancer
- [ ] Esophageal Cancer
- [ ] Fallopian Tube Cancer
- [ ] Gall Bladder / Cholangiocarcinoma
- [ ] Head & Neck: Tongue, Lip, Oropharynx, Nasopharynx
- [ ] Hodgkin's Disease
- [ ] Kidney Cancer
- [ ] Liver Cancer
- [ ] Lung Cancer
- [ ] Lymphoma
- [ ] Melanoma
- [ ] Mesothelioma
- [ ] Multiple Myeloma
- [ ] Non-Melanoma Skin Cancers
- [ ] None
- [ ] Other Cancer
- [ ] Ovarian Cancer / Primary Peritoneal Cancer

- [ ] Pancreatic Cancer
- [ ] Penile Cancer
- [ ] Prostate Cancer
- [ ] Rectal Cancer
- [ ] Sarcoma
- [ ] Stomach Cancer
- [ ] Testicular Cancer
- [ ] Thymoma or Thymic Carcinoma
- [ ] Thyroid Cancer
- [ ] Uterine cancer
- [ ] Vaginal and Vulvar Cancers

Which cancer treatments have you received or are currently receiving? (Please select all that apply.) *

- [ ] Radiation Therapy
- [ ] Chemotherapy
- [ ] Surgery
- [ ] Hormone Treatment
- [ ] Other

The following questions are for patients who have received radiation therapy in the past or are currently receiving radiation therapy.

Have you received or are you currently receiving radiation therapy? *

- (•) Yes
- ( ) No

Please indicate which part of your body has been treated with radiation (please select all that apply): *

- [ ] Brain
- [ ] Head and Neck
- [x] Chest
- [ ] Abdomen
- [ ] Pelvis
- [ ] Arms or Legs
- [ ] Skin
- [ ] None

Where did you receive your radiation treatments? *

- [ ] Academic Medical Center
- [ ] Community Hospital
- [ ] Doctor's office or clinic
- [ ] None

When did you receive your radiation? *

- (•) Currently on treatment
- ( ) Completed within the last 6 months

- Completed 7 months - 2 years ago
- Completed more than 2 years ago
- Never had radiation

Did you develop redness, irritation, or itchiness of the skin with radiation treatments? *

- Yes
- No

How red did your skin become during treatment? *

- Mildly red
- Moderately red
- Very red

Did you develop skin peeling during radiation? *

- Yes
- No

If YES, was the affected skin dry or flaky? *

- Yes
- No

If YES, did the affected skin ever weep or look wet? *

- Yes
- No

Did your healthcare provider recommend that you use creams or other topical treatment for skin irritation caused by your radiation treatments? *

- Yes
- No

Were you ever told by a health care professional to AVOID applying skin creams to the area receiving radiation right before you received your radiation? *

- Yes
- No

Were you ever told by a healthcare professional to AVOID applying skin creams to the area receiving radiation for at least a few hours before you got your radiation? *

- Yes
- No

Were you ever told to wash or wipe off your skin creams before you got radiation? *

- Yes
- No

Were you told to use special soaps on your skin? *

- Yes
- No

Were you treated for breast cancer? *

- Yes
- No

If YES, were you ever told during your treatments to avoid using certain deodorants/antiperspirants under your arm on the side being radiated? *

- (•) Yes
- ( ) No

Who was the main source of information about managing your skin irritation during treatment? *

- ( ) Nurse
- ( ) Nurse practitioner
- (•) Physician

What skin treatments did you use for your radiation skin reaction (can select multiple)? *

- [ ] Aquaphor
- [ ] Radiagel
- [ ] Eucerin
- [ ] Glaxal
- [ ] Silver sulfadiazine cream (Silvadene or Flamazine)
- [ ] Hydrocortisone cream (Cortizone cream or CortAid)
- [ ] Cornstarch
- [ ] Domeboro
- [ ] Aquaphor with lidocaine (numbing agent)
- [ ] Coco Butter
- [ ] Zinc oxide cream
- [ ] Generic Moisturizer
- [ ] Other

Severity of Symptoms

Please indicate the severity of your radiation-related skin irritation at its worst on a scale from 0 to 5 where 0 is “no symptoms” and 5 represents “severe symptoms”

Burning: *

- ( ) 0
- ( ) 1
- ( ) 2
- ( ) 3
- ( ) 4
- ( ) 5

Itchiness: *

- ( ) 0
- ( ) 1
- ( ) 2
- ( ) 3
- ( ) 4
- ( ) 5

Tightness or pulling sensation: *

- 0
- 1
- 2
- 3
- 4
- 5

Tenderness: *

- 0
- 1
- 2
- 3
- 4
- 5

Other sypmptoms: *

- 0
- 1
- 2
- 3
- 4
- 5

Please check.

I'm not a robot reCAPTCHA Privacy - Terms

Submit Your Answers Now

Subscribe to our newsletters.

Email Address

OncoLink eNewsletters

- [x] **Array**
- [ ] **Array**

Subscribe Now

Recent Posts

Nutrition During Proton Therapy For Kids (http://www.oncolink.org/blogs/2017/04/nutrition-proton-therapy-kids/)

There's an App for That- Medication Reminders (http://www.oncolink.org/blogs/2017/03/theres-app-medication-reminders/)

Cancer Makes Everyone Stupider – and Smarter (http://www.oncolink.org/blogs/2017/03/cancer-makes-everyone-stupider-smarter/)

It's Not All Rainbows and Glitter (http://www.oncolink.org/blogs/2017/03/not-rainbows-glitter/)

The Skinny on Soy and Flaxseed for Breast Cancer (http://www.oncolink.org/blogs/2017/03/skinny-soy-flaxseed-breast-cancer/)

Forums

Forum Support (http://www.oncolink.org/blogs/forums/forum/forum-support/)

O-PRO Forum (http://www.oncolink.org/blogs/forums/forum/introduction-to-the-forum/)

Quick Links

Cancer Types

Risk and Prevention

Healthcare Professionals

Cancer Treatment

Support

Caregivers

OncoLink Penn Medicine est. 1994

About OncoLink (/about)

How to Partner (/about/how-to-partner-with-oncolink)

Mission Statement (/about/mission-statement)

Editorial Board (/about/oncolink-editorial-board)

Use of OncoLink Content (/about/use-of-the-oncolink-site-and-content)

Contact Us (/about/contact-information)

Giving to OncoLink (/about/giving-to-oncolink)

Link to OncoLink (/about/link-to-oncolink)

Privacy Statement (/about/privacy-statement)

Disclaimer (/about/general-disclaimer)

(http://www.facebook.com/oncolink) (http://twitter.com/oncolinkteam) (https://plus.google.com/u/0/100521024587203821368/posts) (http://www.vimeo.com/oncolink)

Skin cream usage for radiation-related skin reactions: An internet-based provider survey

The following survey will help us to better understand current practices and attitudes among healthcare providers regarding skin cream usage for radiation dermatitis. We will also ask a few other general questions related to how you manage skin care and radiation.

This anonymous online survey contains 18 multiple choice questions. There is no time limit, though some people take about 5 minutes to complete the survey.

Contacts and Questions

Principal Investigator: James Metz, MD

Co-investigator: Brian Baumann, MD

All questions or other comments may be sent to Brian Baumann at the following:

Email: Brian.Baumann@uphs.upenn.edu
Phone Number: 215-662-2428

If you have questions about your rights as a research subject you may contact the Office of Regulatory Affairs at 215-898-2614.

Statement of Consent

Completion of the following survey indicates my consent to participate.

Statement of Consent *

Completion of the following survey indicates my consent to participate.

☐ I have read the above information and I feel I understand the study well enough to make a decision about my involvement.

Please indicate your role as a healthcare provider: *

- ○ Nurse
- ○ Nurse practitioner
- ◉ Physician

Please indicate your field in oncology: *

- ◉ Radiation Oncology
- ○ Medical Oncology
- ○ Surgical Oncology
- ○ Dermatology
- ○ Other Please Specify

Please indicate the type of practice where you work: *

- ○ Academic Medical Center
- ○ Community Hospital
- ○ Doctor's Office or Clinic
- ○ Other Please Specify

Are you ever involved in managing or helping to manage your patient's radiation dermatitis? *

- (•) Yes
- ( ) No

Do you ever advise patients NOT to apply certain skin creams, particularly those containing metals e.g. zinc oxide or silver sulfadiazine cream (Silvadene) just prior to radiation or within a few hours before radiation? *

- (•) Yes
- ( ) No

Do you ever advise patients NOT to apply skin moisturizers just prior to radiation or within a few hours before radiation? *

- (•) Yes
- ( ) No

Why do you recommend that patients NOT apply SKIN MOISTURIZERS before radiation treatment? (Please select all that apply): *

- [ ] Concern that creams might cause a bolus effect and increase the skin dose
- [ ] Routine clinical practice
- [ ] Not applicable, I do not recommend this

Why do you recommend that patients NOT apply METAL-CONTAINING SKIN CREAMS before radiation? (please select all that apply): *

- [ ] Concern that the thickness of creams might cause a bolus effect and increase the skin dose
- [ ] Concern that scattered low energy electrons caused by metals in some creams might increase skin dose
- [ ] Routine clinical practice
- [ ] Not applicable, I do not recommend this

Do you make recommendations on specific soaps that patients should or should not use during radiation? *

- (•) Yes
- ( ) No

Do you ever tell certain patients (e.g. breast cancer patients) not to apply particular deodorants or antiperspirants? *

- (•) Yes
- ( ) No

Do you ever tell these patients to avoid aluminum-containing deodorants or antiperspirants? *

- (•) Yes
- ( ) No

Are you Radiation Oncologist? *

- (•) Yes
- ( ) No

The following questions relate to patients undergoing post-mastectomy radiation:

The following questions should be completed by radiation oncologists only. If you reached this page in error, please correct the above question (answer "no").

Do you treat with bolus on the skin? *

- (•) Yes
- ( ) No

If yes, do you use daily bolus? *

- (•) Yes
- ( ) No

Bolus thickness for daily bolus? *

- ( ) 0.5 cm

1.0 cm

Other Please Specify

Do you use every other day bolus? *

Yes

No

Bolus thickness for every other day bolus? *

0.5 cm

1.0 cm

Other Please Specify

Do you routinely bolus the skin after positive neck dissections for patients with head and neck cancers? *

Yes

No

How do you typically treat acute Grade 3 radiation dermatitis (confluent moist desquamation >1.5 cm in diameter and not confined to skin folds and/or pitting edema)? (select all that apply): *

Moisturizer (e.g. Aquaphor, Radiagel, Eucerin)

Moisturizer with Lidocaine

Domeboro

Silvadene Cream

Hydrocortisone cream

Oral pain medication

Oral steroids

Specialized dressings bandages (e.g. Telfa, hydrocolloid dressings like DuoDERM, Xeroform gauze)

Other

Submit Your Answers Now

Recent Posts

How Much Do You Really Know About Testicular Cancer? (http://www.oncolink.org/blogs/2017/04/much-really-know-testicular-cancer/)

Nutrition During Proton Therapy For Kids (http://www.oncolink.org/blogs/2017/04/nutrition-proton-therapy-kids/)

There's an App for That- Medication Reminders (http://www.oncolink.org/blogs/2017/03/theres-app-medication-reminders/)

Cancer Makes Everyone Stupider – and Smarter (http://www.oncolink.org/blogs/2017/03/cancer-makes-everyone-stupider-smarter/)

It's Not All Rainbows and Glitter (http://www.oncolink.org/blogs/2017/03/not-rainbows-glitter/)

Forums

Forum Support (http://www.oncolink.org/blogs/forums/forum/forum-support/)

O-PRO Forum (http://www.oncolink.org/blogs/forums/forum/introduction-to-the-forum/)

Quick Links

Cancer Types

Risk and Prevention

Healthcare Professionals

Cancer Treatment

Support

Caregivers

OncoLink Penn Medicine est. 1994

About OncoLink (/about)

How to Partner (/about/how-to-partner-with-oncolink)

Mission Statement (/about/mission-statement)

Editorial Board (/about/oncolink-editorial-board)

Use of OncoLink Content (/about/use-of-the-oncolink-site-and-content)

Contact Us (/about/contact-information)

Giving to OncoLink (/about/giving-to-oncolink)

Link to OncoLink (/about/link-to-oncolink)

Privacy Statement (/about/privacy-statement)

Disclaimer (/about/general-disclaimer)

(http://www.facebook.com/oncolink) (http://twitter.com/oncolinkteam) (https://plus.google.com/u/0/100521024587203821368/posts) (http://www.vimeo.com/oncolink)