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UNITED STATES OF AMERICA
NUCLEAR REGULATORY COMMISSION

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ADVISORY COMMITTEE ON THE MEDICAL USES OF ISOTOPES

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TELECONFERENCE

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THURSDAY, FEBRUARY 15, 2018

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The meeting was convened at 9:06 a.m., Philip Alderson, ACMUI
Chairman, presiding.

MEMBERS PRESENT:

- PHILIP O. ALDERSON, M.D., Chairman
- VASKEN DILSIZIAN, M.D., Nuclear Cardiologist
- RONALD D. ENNIS, M.D., Radiation Oncologist
- DARLENE F. METTER, M.D., Diagnostic Radiologist
- MICHAEL O'HARA, Ph.D., FDA Representative
- CHRISTOPHER J. PALESTRO, M.D., Nuclear Medicine
Physician
- MICHAEL A. SHEETZ, Radiation Safety Officer
- JOHN J. SUH, M.D., Radiation Oncologist
- LAURA M. WEIL, Patients' Rights Advocate
- PAT B. ZANZONICO, Ph.D., Vice Chairman

NON-VOTING MEMBERS PRESENT:

RICHARD GREEN

MEGAN SHOBER

ZOUBIR OUHIB

NRC STAFF PRESENT:

CHRISTIAN EINBERG, Acting Deputy Director, NMSS/MSST

DOUGLAS BOLLOCK, ACMUI Designated Federal
Officer

SOPHIE HOLIDAY, ACMUI Alternate Designated
Official and ACMUI Coordinator

MARYANN AYOADE, NMSS/MSTR/MSEB

JENNIFER BISHOP, R-III/DNMS

SAID DAIBES, Ph.D., NMSS/MSST/MSEB

JASON DRAPER, R-III

SARA FORSTER, R-III/DNMS

CASSANDRA FRAZIER, R-III/DNMS

MICHELLE HAMMOND, R-IV/DNMS

VINCENT HOLAHAN, Ph.D., NMSS/MSST

PATRICIA JEHLE, OGC

JAN NGUYEN, RI/DNMS

PATTY PELKE, R-III/DNMS

GRETCHEN RIVERA-CAPELLA, NMSS/MSST/MSEB

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NRC STAFF PRESENT (CONT.):

LAURA SHRUM, OGC

DANIEL STROHMEYER, R-III/DNMS

KATHERINE TAPP, Ph.D., NMSS/MSTR/MSEB

FRANK TRAN, R-III/DNMS

LESTER TRIPP, R-I/DNMS

IRENE WU, NMSS/MSST/MSEB

MEMBERS OF THE PUBLIC:

BETTE BLANKENSHIP, American Association of Physicists
in Medicine (AAPM)

KELLY CLASSIC, Mayo Clinic

CHARLES CODLEMAN, VA Radioactive Materials Program

THOMAS CONLEY, University of Kansas Medical Center

Whitney Cox, Illinois (IL) Emergency Management
Agency

ROBERT DANSEREAU, New York State (NYS) Department of
Health

ARIEL DOUCET, Virtua Health

ADAM EKSTEDT, IL Emergency Management Agency

ASFAW FENTA, Virginia (VA) Radioactive Materials
Program

MICHAEL FULLER, VA Radioactive Materials Program

MIGUEL DE LA GUARDIA, Cook Children's Health Care
System

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MEMBERS OF THE PUBLIC (CONT.):

SANDRA GABRIEL, *unaffiliated*

JERRY GEORGE, Baptist Health South Florida

KIMBERLY GILLIAM, VA Radioactive Materials Program

THEODORE GODFREY, Elekta, Inc.

BENNETT GREENSPAN, Society of Nuclear Medicine and
Molecular Imaging (SNMMI)

STANLEY HAMPTON, Eli Lilly and Company

STEVE HARRISON, VA Radioactive Materials Program

DESIREE KENNEDY, Elekta, Inc.

RICHARD KENNEY, *unaffiliated*

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CAROL MARCUS, University of California at Los Angeles

RICHARD MARTIN, American Association of Physicists in
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CATHERINE PERHAM, Maine Radiation Control Program

RICHARD PEROS, New Jersey Radioactive Materials
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MEMBERS OF THE PUBLIC (CONT.):

ERIC PERRY, Kentucky Radioactive Materials Section

MICHAEL PETERS, American College of Radiology (ACR)

BRUCE PROCTOR, Elekta.Inc.

BRAD READ, Elekta, Inc.

SYLVIA REVELL, University of Texas Southwestern
Medical School

DANIEL SAMSON, NYS Department of Health

BETH SCHILKE, VA Radioactive Materials Program

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LOU SHIMABUKU, *unaffiliated*

EUGENIO SILVERSTRINI, Northwell Health

MICHAEL STABIN, Vanderbilt University

CINDY TOMLINSON, American Society of Radiation
Oncology (ASTRO)

MICHAEL WELLING, University of Virginia

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P-R-O-C-E-E-D-I-N-G-S

(9:06 a.m.)

CHAIRMAN ALDERSON: Well, good morning, and welcome to today's ACMUI public teleconference. We'll discuss two topics today: nursing mothers' guidelines, the subcommittee report; and the physical presence requirements for the gamma knife, also a subcommittee report.

I will now turn it over to Mr. Doug Bollock from the NRC for some opening remarks.

MR. BOLLOCK: Thank you, Dr. Alderson. Good morning. As the designated federal officer for this meeting, I am pleased to welcome you to the public meeting of the Advisory Committee on Medical Uses of Isotopes.

My name is Doug Bollock. I am the chief of the Medical Safety and Events Assessment Branch, and I have been designated as the federal officer for this Advisory Committee in accordance with 10 CFR Part 7.11.

Present today as the alternate designated federal officer is Sophie Holiday, our ACMUI coordinator.

This announced meeting of the Committee is being held in accordance with the rules and

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1 regulations of the Federal Advisory Committee Act and
2 the Nuclear Regulatory Commission. This meeting is
3 being transcribed by the NRC, and it may also be
4 transcribed or recorded by others. This meeting was
5 announced in the January 23, 2018, edition of the
6 Federal Register on 83 page 3191.

7 The function of the Committee is to advise
8 the staff on issues and questions that arise on
9 medical uses of byproduct material. The Committee
10 provides counsel to the staff but not determine or
11 direct the actual decisions of the staff or the
12 Commission. The NRC solicits the view of the
13 Committee and values their opinion.

14 I request that whenever possible we try
15 to reach a consensus on the various issues that we
16 will discuss today. But I also recognize there may
17 be minority or dissenting opinions. If you have such
18 opinions, please allow them to be read into the
19 record.

20 At this point, I'd like to perform a roll
21 call of the ACMUI members participating today. Dr.
22 Philip Alderson?

23 CHAIRMAN ALDERSON: Here.

24 MR. BOLLOCK: Thank you. Dr. Pat
25 Zanzonico?

1 VICE CHAIRMAN ZANZONICO: Yes.

2 MR. BOLLOCK: Thank you. Dr. Vasken
3 Dilsizian?

4 MEMBER DILSIZIAN: Here.

5 MR. BOLLOCK: Dr. Ronald Ennis?

6 MEMBER ENNIS: Here.

7 MR. BOLLOCK: Thank you. Dr. Darlene
8 Metter?

9 MEMBER METTER: Here.

10 MR. BOLLOCK: Thank you. Dr. Michael
11 O'Hara?

12 MEMBER O'HARA: Here.

13 MR. BOLLOCK: Thank you. Dr. Christopher
14 Palestro?

15 MEMBER PALESTRO: Here.

16 MR. BOLLOCK: Thank you. Mr. Michael
17 Sheetz?

18 MEMBER SHEETZ: Here.

19 MR. BOLLOCK: Thank you. Dr. John Suh?

20 MEMBER SUH: Here.

21 MR. BOLLOCK: Thank you. And Ms. Laura
22 Weil.

23 MEMBER WEIL: Here.

24 MR. BOLLOCK: Thank you. I've confirmed
25 that a quorum is met by the presence of at least six

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1 members.

2 Also, on the phone do we have Mr. Zoubir
3 Ohib?

4 MR. OUHIB: Here.

5 MR. BOLLOCK: Thank you. Mr. Richard
6 Green?

7 MR. GREEN: Here.

8 MR. BOLLOCK: Thank you. And Ms. Megan
9 Shober?

10 MS. SHOBER: Here.

11 MR. BOLLOCK: All right. Thank you.

12 Mr. Ouhib has been selected as ACMUI's
13 therapy medical physicist. Mr. Green has been
14 selected as the ACMUI nuclear pharmacist. And Ms.
15 Shober has been selected as the ACMUI Agreement State
16 Representative.

17 At this time, Mr. Ouhib, Mr. Green, and
18 Ms. Shober are pending security clearance but may
19 participate in the meeting. However, they do not
20 have voting rights at this time.

21 I now ask NRC staff members who are
22 present to identify themselves. I'll start with
23 individuals in the room here.

24 MS. HOLIDAY: Sophie Holiday, ACMUI
25 coordinator.

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1 DR. TAPP: Dr. Katie Tapp with the medical
2 team.

3 MS. WU: Irene Wu with the medical team.

4 DR. HOLAHAN: Dr. Vincent Holahan, senior
5 advisor.

6 MR. BOLLOCK: Okay. Now we go to NRC
7 employees on the phone.

8 MR. BOLLOCK: Maryann, are you with us?

9 MS. AYOADE: Yes, I am. I had you on
10 mute. Here.

11 MR. BOLLOCK: Okay. That's Maryann
12 Ayoade, also with the medical team.

13 MS. AYOADE: That's correct.

14 MR. BOLLOCK: Anyone else? Any other NRC
15 headquarters employees on the phone?

16 Okay. Are there any NRC regional
17 employees on the phone?

18 Okay. Thank you all. Members of the
19 public who notified Ms. Holiday that they would be
20 participating on the teleconference will be captured
21 in the transcripts. Those of you who did not provide
22 prior notification, please contact Ms. Holiday at
23 sophie.holiday@nrc.gov. That's S-O-P-H-I-E dot H-O-
24 L-I-D-A-Y at N-R-C dot G-O-V. Or call her at
25 (301) 415-7865.

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1 We have a bridge line available, and that
2 phone number is (888) 790-6447. The passcode to
3 access the bridge line is 279-0867 followed by the
4 pound key.

5 This meeting is also using to the GoTo
6 webinar application to view the presentation handouts
7 real time. You can access this by going to
8 www.gotowebinar.com, G-O-T-O-W-E-B-I-N-A-R dot com
9 and searching for the meeting ID 563-775-347.

10 The purpose of this meeting is to discuss
11 the revised draft report for the ACMUI nursing mother
12 guidelines for the medical administration of
13 radioactive materials, and the revised draft report
14 for the ACMUI physical presence requirements for the
15 Leksell Gamma Knife® Icon™.

16 Individuals who would like to ask a
17 question or make a comment regarding a specific issue
18 the committee has discussed should request permission
19 to be recognized by the ACMUI chairperson, Dr. Philip
20 Alderson. Dr. Alderson, at his option, may entertain
21 comments or questions from members of the public who
22 are participating with us today.

23 Comments and questions are usually
24 addressed by the Committee near the end of the
25 presentation after the Committee has fully discussed

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1 the topic. We ask that one person speak at a time as
2 this meeting is also closed caption.

3 I would also like to add that handouts and
4 an agenda for this meeting are available on the NRC's
5 public website.

6 At this time, I'd ask that everyone on the
7 call who is not speaking to place their phones on
8 mute. If you do not have the capability to mute your
9 phone, please press star six to utilize the
10 conference line mute and unmute function.

11 I would ask everyone to exercise care to
12 ensure that background noise is kept at a minimum, as
13 any stray background sounds can be very disruptive on
14 a conference call this large.

15 At this point, I would like to turn the
16 meeting back over to Dr. Alderson.

17 CHAIRMAN ALDERSON: Thank you, Mr.
18 Bollock. So I will then start the meeting by turning
19 it to Dr. Darlene Metter, who is the chair of the
20 Nursing Mothers Guidelines Subcommittee. Dr. Metter?

21 MEMBER METTER: Thank you, Dr. Alderson.
22 And I'd like to first thank the work of my
23 subcommittee members, Dr. Vasken Dilsizian, Dr.
24 Christopher Palestro, and Dr. Pat Zanzonico.

25 The subcommittee charge was to review the

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1 radiation exposure from diagnostic and therapeutic
2 radiopharmaceuticals, including brachytherapy, to
3 the nursing mother and child.

4 Now, as a summary of our report in
5 September, we know that many drugs and
6 radiopharmaceuticals administered to the nursing
7 mother can enter her milk, and then, therefore, be
8 ingested by the nursing child. The subcommittee
9 recommendations regarding the radiation exposure to
10 the nursing child follows current existing
11 recommendations for the nursing mother by reputable
12 expert sources such as the NRC, ICRP, Dr. Michael
13 Stabin's paper, and others.

14 Therefore, our subcommittee
15 recommended -- recommendations mirrored the sources
16 with the use of a maximum dose of 100 millirem to the
17 nursing child. The current literature at times had
18 variable recommendations on the temporary
19 interruption of breastfeeding due to
20 radiopharmaceuticals in the mother's milk, and the
21 subcommittee generally opted to choose the most
22 conservative, which was usually the longest
23 interruption period.

24 The subcommittee results and
25 recommendations are summarized in a table reviewed at

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1 the September 2017 ACMUI meeting. Since that time,
2 there have been comments from Dr. Carol Marcus and
3 Dr. Michael Stabin, and Dr. Bennett Greenspan and the
4 SNMMI. To review these comments, Dr. Pat Zanzonico
5 will address them and the associated report
6 revisions.

7 Dr. Zanzonico?

8 VICE CHAIRMAN ZANZONICO: Thank you, Dr.
9 Metter. So as Dr. Metter just said, we received a
10 number of comments, both from Drs. Marcus and Stabin,
11 and independent from Dr. Greenspan and the Society of
12 Nuclear Medicine and Molecular Imaging. So what I
13 was going to do was step through their respective
14 comments and summarize our responses.

15 This was an information-dense report, and
16 so there were a number of comments, so please bear
17 with me. The first comment from Drs. Marcus and
18 Stabin was that the draft report failed to describe
19 or at least acknowledge the real and significant
20 benefits of breastfeeding to both the infant and the
21 nursing mother, and they include a statement from the
22 American Academy of Pediatrics to that effect.

23 And that point is well taken, and in our
24 subsequent revision of the report we think it would
25 be reasonable to include a statement explicitly

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1 acknowledging the benefits of breastfeeding to the
2 mother and child, and so we plan to do that in the
3 revised -- the subsequent revision of our report.

4 The second point was that the so-called
5 specific gamma ray factors cited in Table 2 are
6 incorrect. They indicate by a factor of 1,000. And
7 this was a units transcription error. The values in
8 the table, and as used in our calculations, are in
9 roentgen centimeters squared per microcurie hour.

10 The mu for micro when it went to hard copy
11 became an 'm' for milli inadvertently. And so the
12 factor of 1,000 error was apparent. We will correct
13 that, of course, in the subsequent revision, but I
14 want to assure everyone that the actual calculations
15 and analyses were based on the actual correct values.

16 I will just also address the related point
17 of a comment by Dr. Greenspan and the SNMMI. They
18 state in their comments that the specific gamma ray
19 constant, the quantities I'm referring to right now,
20 were in error, and they provided a number of different
21 values with variable units being used.

22 And of course if we have numerical or
23 other factual errors in the report, those will be
24 corrected and reflected in a revised analysis.
25 However, we asked that Dr. Greenspan and the SNMMI

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1 provide a reference for their values. No such
2 reference was provided with their written comments,
3 and so we have no way at this point of verifying their
4 veracity, their accuracy.

5 Our specific gamma ray constants were
6 taken from a classic textbook in medical physics,
7 Johns and Cunningham, which many of you may be
8 familiar with. So that's the source of our data, but
9 we understand that specific gamma ray constants, like
10 other physical quantities, are periodically updated,
11 and we certainly want to use the most current and
12 most accurate values in our analysis.

13 And if Dr. Greenspan and the Society can
14 provide a reference, so that we can verify the
15 accuracy of their stated values, we will amend our
16 report accordingly.

17 The next point from Drs. Marcus and Stabin
18 was they found a number of typos and editorial errors,
19 and we appreciate, of course, their careful reading
20 of the report as we appreciate all their comments and
21 insights, and we will certainly correct these
22 editorial errors in the subsequent revision.
23 Likewise, Dr. Greenspan and the Society noted a
24 number of editorial errors, and we will correct those
25 as well, of course.

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1 One issue that arose, which is always a
2 thorny one, is the system of units to use. We use
3 essentially conventional units because, frankly,
4 that's the system of units most of us, including
5 myself, are most familiar with and most comfortable
6 with. But we certainly appreciate that we should be
7 transitioning to use of SI units.

8 And we will confirm with the NRC staff to
9 verify that that's an appropriate thing to do, and
10 we'll amend our report accordingly to use SI rather
11 than conventional units or perhaps SI units primarily
12 with conventional units presented parenthetically.
13 But we will address that point.

14 A fourth point raised by Drs. Marcus and
15 Stabin was that the dosimetry analysis for
16 radioiodines, specifically with respect to the
17 thyroid, used worst-case factors in terms of maximal
18 uptakes of radioiodine by the thyroid and minimal
19 thyroid gland masses. Both of those conservative
20 assumptions would lead to maximal estimates of
21 dosimetry.

22 And Drs. Marcus and Stabin recommended
23 that we perform this thyroid dosimetry analysis for
24 all medically used radioiodines, not just I-131. So
25 that would include, of course, I-123, nowadays I-124,

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1 perhaps even I-125. And they also suggested that in
2 that analysis we use a range of uptakes, not simply
3 maximal uptake, and a range of age-dependent uptakes
4 and age-dependent thyroid masses. And we can
5 certainly do that.

6 And, immodestly, I cite my own paper, Age-
7 Dependent Thyroid-Absorbed Doses for
8 Radiobiologically Significant Radioisotopes of
9 Iodine from Health Physics, 2000. So we can extract
10 dose estimates or -- in the dosimetry analysis from
11 that paper and incorporate the suggested, augmented
12 analysis in the subsequent revision of our report.

13 Drs. Marcus and Stabin also point out that
14 two significant literature references were not cited
15 in the paper, and certainly we want to be as
16 comprehensive and thorough as possible in
17 incorporating the pertinent scientific literature
18 into our recommendations. And we will certainly
19 review these papers and incorporate them, at least
20 cite them, in our report and, if necessary, make
21 whatever adjustments those dictate.

22 And they also point out that perhaps an
23 ill-advised phrase was included in the report
24 referencing the available scientific literature on
25 breastfeeding, dosimetry, and so forth; namely, the

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1 phrase being the general lack of pertinent data in
2 the literature. And on further reflection, I think
3 we all acknowledge -- and you can verify this by
4 looking at the bibliography -- the references in our
5 report, there actually is already significant
6 literature on the subject. So we will eliminate that
7 phrase as well as include these additional
8 references.

9 A further point that was made is that
10 rather than using or modeling the mother and the
11 mother's breast as point sources -- and that is often
12 done, frankly, for simplicity purposes in dose
13 calculations -- we modeled those source regions in
14 terms of the external dose to the nursing baby. We
15 modeled those as line sources based on a paper in the
16 literature, and that yields a more realistic estimate
17 of the external dose to the infant than does a point
18 source model.

19 Drs. Marcus and Stabin point out, however,
20 that there are so-called humanized gamma ray
21 constants available, certainly at least for I-131.
22 However, we point out -- or we would like to point
23 out that in our calculation we not only model the
24 mother's body and breast as line sources, but we also
25 incorporated the self-absorption of extant gamma rays

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1 by those respective source regions, and we also --
2 well, we modeled those, as I say, as attempting to
3 count the self-absorption.

4 So we think that our approach, even though
5 we use specific gamma ray constants which implicitly
6 implies -- which implies a point source, we think
7 we've made the necessary adjustments to appropriately
8 quote/unquote "humanize our specific gamma ray
9 constant values."

10 I'm just thumbing through my notes.
11 Another point that was made -- and this was a lengthy,
12 very scholarly comment, indicating that basing
13 recommendations with regard to cessation of
14 breastfeeding for mothers who undergo a nuclear
15 medicine procedure, basing that on a 100 millirem
16 limit to the nursing infant is overly conservative,
17 and Drs. Marcus and Stabin recommend a dose limit of
18 five millisieverts instead.

19 And incorporated into that comment was a
20 strong reputation of the linear non-threshold dose
21 response model for cancer induction by radiation.
22 And I think many of us, myself included, are very
23 empathetic so to speak to that point, and I think
24 many of us have well-founded skepticism about the
25 biological validity of the linear non-threshold

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1 model.

2 But having said that, really, a discussion
3 of that model, as important and interesting as it is
4 certainly, is really beyond the scope of our report.
5 And as Dr. Metter pointed out, we deferred to the
6 prevailing recommendations made by authoritative
7 bodies like the ICRP, NCRP, and so forth.

8 And we also noted that in their original
9 analysis, in the really seminal and widely cited
10 paper by Dr. Stabin and Dr. Bryce, that they based
11 their analysis on a one millisievert effective dose
12 quote/unquote limit to the nursing infant.

13 So based on all of those considerations,
14 and despite our misgivings of the linear non-
15 threshold dose-response models, we decided, as
16 Dr. Metter indicated, to use a one millisievert limit
17 upon which to base our recommendations.

18 Proceeding now to the comments submitted
19 by Dr. Greenspan and the Society, to address their
20 comment on the possible -- possibly erroneous
21 specific gamma ray constant values, and we will ask
22 them and await the literature citation of the values
23 they cite, and based on our subsequent review of these
24 values in that literature adjust the specific gamma
25 ray constants and our values and our calculations

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1 accordingly.

2 I mentioned that they also had a number
3 of editorial corrections which we will certainly
4 address in a subsequent revision of the paper. And
5 there was a question or a disagreement with our
6 recommendation for discontinuing of breastfeeding
7 following administration of I-123 labeled
8 radiopharmaceuticals, not only sodium iodide but also
9 ortho-iodohippurate and MIGB,
10 metaiodobenzylguanidine, which are all used
11 clinically labeled with I-123.

12 And I think there may have been a
13 misunderstanding, understandably, given all of the
14 numbers and so forth in the paper, in the report
15 rather, but in Table 2 -- I'm sorry, in Table 5 of
16 the report, in which we include our recommendations
17 on cessation, the penultimate column, the next-to-
18 last column, which uses the -- which lists the current
19 recommendations of -- that we use here at Memorial
20 Sloan Kettering, indicated a seven-day
21 discontinuation following administration of at least
22 certain I-123 radiopharmaceuticals.

23 But if you looked at the recommendations
24 for -- from the Committee, which is actually in the
25 very last column of that table, our recommendations

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1 are much shorter, no more than 48 hours, and in the
2 case of I-123, iodohippurate, not recommending any
3 interruption of breastfeeding.

4 So I think we have all -- I think what we
5 -- what the committee or subcommittee has recommended
6 is perfectly consistent with the point that Dr.
7 Greenspan and the Society were making. So, yes, as
8 you see what's on the screen now, in the very last
9 column, the fourth, fifth, and sixth lines refer to
10 cessation of I-123, sodium iodide;
11 metaiodobenzylguanidine, MIGB; and the last of those
12 three lines, line 6, to ortho-iodohippurate labeled
13 with I-123. So I think our recommendations are
14 consistent with what the Society is recommending.

15 Dr. Greenspan and the Society are also
16 recommending a more thorough, a more complete
17 dosimetric analysis of radioiodine as a function of
18 age, child age, and thyroid mass. And as I alluded
19 to earlier, we will provide an expanded dosimetric
20 analysis as also recommended by Drs. Marcus and
21 Stabin.

22 And Dr. Greenspan and the Society also
23 forcefully endorsed the recommendation of Drs. Marcus
24 and Stabin that, number one, a 500 millirem rather
25 than a 100 millirem dose limit or dose benchmark upon

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1 which to base recommendations is more appropriate,
2 and that the linear non-threshold model is really not
3 only inappropriate but incorrect.

4 So I have already addressed that point in
5 my earlier comments. And so that actually completes
6 our point-by-point response to the submitted
7 comments, both by Drs. Marcus and Stabin, and by Dr.
8 Greenspan and the Society. We very much appreciate
9 their careful and thoughtful -- their careful reading
10 of the report and their thoughtful comments. And we
11 have tried to address them as comprehensively as
12 possible. And I think we've done so and will revise
13 the report accordingly.

14 So that concludes my comments in terms of
15 our responses to the submitted comments. So, Dr.
16 Metter, I will turn it back to you.

17 MEMBER METTER: Thank you, Dr. Zanzonico,
18 for a very thorough review and work on the comments
19 from Drs. Marcus, Stabin, Greenspan, and the Society
20 of Nuclear Medicine.

21 Do I have other comments from our
22 subcommittee members?

23 Okay. Hearing none --

24 MEMBER WEIL: Dr. Metter?

25 MEMBER METTER: Yes.

1 MEMBER WEIL: This is Laura Weil. I do
2 have a comment, and I'd like to apologize for not
3 submitting it in advance. The subcommittee report
4 recommends the complete cessation of -- states that
5 the cessation of milk production generally occurs
6 about six weeks after the last breastfeeding.

7 And I encountered a report from the ATA,
8 which recommends a longer period of cessation, and
9 I'd like to -- this is from the ATA from 2009 in
10 Thyroid. If I might just briefly read this paragraph
11 and ask for an evaluation of it, basically.

12 Let's see. Breastfeeding must be stopped
13 at least six weeks before administration of I-131
14 therapy, and a delay of three months will more
15 reliably ensure that lactation-associated increase in
16 breast sodium iodide symporter activity has returned
17 to normal.

18 I wonder if six weeks in our -- in the
19 subcommittee report could be amended to at least six
20 weeks in order to acknowledge the potential for a
21 longer period of time being necessary. I don't know
22 how one would assess how long a period of time between
23 six weeks and three months should be recommended, but
24 certainly for the provision of information to
25 patients, in accordance with the ALARA principles, so

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1 that breastfeeding women would have time to allow at
2 least six weeks' cessation of breastfeeding before
3 administration of Iodine-131. Would you comment on
4 that?

5 MEMBER METTER: Yes. Actually, thanks for
6 bringing that up. There was a comment as far as the
7 minimal timeframe in regards to notifying the nursing
8 mother regarding her I-131 therapy issue with
9 nursing, and we did say it was going to be at six
10 weeks. I have no problem saying at least six weeks
11 prior to the radioiodine administration. Does
12 anybody else on the subcommittee have any comments?

13 VICE CHAIRMAN ZANZONICO: This is Pat
14 Zanzonico. I have no problem either with that
15 language, meaning specifically 'at least six weeks.'
16 I think we all recognize that both medically and
17 logistically the longer that period of
18 discontinuation of breastfeeding begins prior to
19 therapy, the more problematic it becomes.

20 And so I think six weeks itself may be
21 somewhat problematic, but I have no problem at all
22 with that language, at least -- at least six weeks
23 for cessation prior to therapy.

24 MEMBER METTER: Thank you, Dr. Zanzonico.
25 Thank you as well for your comment on that. And any

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1 other comments?

2 Okay. Dr. Alderson, I'll turn it back to
3 you.

4 CHAIRMAN ALDERSON: Well, thank you. I
5 believe that must conclude this report and
6 discussion. Are there other comments from people who
7 are online?

8 OPERATOR: And if you have a question or
9 a comment from the phones, you may press star one at
10 this time. Make sure your phone is unmuted and record
11 your name. And to withdraw that request, you may
12 press star two. Once again, press star one for
13 questions or comments from the phones, and I'll stand
14 by for questions or comments.

15 One moment. And we do have a question or
16 comment coming from Carol Marcus. Your line is open.

17 DR. MARCUS: Thank you. Pat, I think
18 we're in complete agreement on everything except the
19 500 millirem calculations. And I think it would be
20 really helpful to have both the 100 millirem and the
21 500 millirem, recognizing that for 21 years the limit
22 has been 500 millirem, and then the physician and the
23 lactating mother decide what ALARA provision is
24 appropriate.

25 Otherwise, what we have is something so

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1 conservative that I think a lot of people won't want
2 to use it. I know that Mike and Hazel's paper
3 originally used 100 millirem, but Mike has changed
4 his mind and thinks 500 millirem calculations would
5 be good. And I think having both might be the best
6 way to do it. Then licensees can choose what seems
7 most appropriate, and we'll have at least the
8 calculations with which to make a good choice.

9 Thank you.

10 OPERATOR: Does that conclude the question
11 or comment?

12 DR. MARCUS: Yes, it does.

13 MEMBER METTER: May I say something on
14 this regarding -- in our paper, the first part as far
15 as the current guidance, it does allude to a nursing
16 mother who has received information that until
17 byproduct material can be released by a licensee, the
18 total effective dose equivalent to any other
19 individual, including her nursing child, is projected
20 to not exceed five millisieverts. But she must give
21 guidance if it's going to exceed one millisievert.
22 So we have that in our paper.

23 DR. MARCUS: Yes. But you don't have the
24 calculations.

25 VICE CHAIRMAN ZANZONICO: This is Pat

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1 Zanzonico. I personally have no objections to
2 including a -- essentially a dual set of
3 recommendations. I mean, the heart of the report and
4 the key recommendations, of course, are the
5 recommendations for the duration of discontinuing
6 breastfeeding.

7 And we can certainly add an additional
8 column which gives those periods of time for a
9 100 millirem dose to the nursing infant and a 500
10 millirem dose to the nursing infant.

11 If I understand correctly, the NRC
12 obviously doesn't regulate breastfeeding, and we can
13 provide, as points of information, the recommended
14 discontinuation periods for 100 and 500 millirem
15 limits, and the patient and their caregivers can then
16 choose as appropriate.

17 I have no objection, scientific or
18 otherwise, to that approach. I don't know if -- if
19 having dual recommendations in effect is problematic
20 from the NRC's point of view. But from a logistical,
21 scientific point of view, I have no objection to that
22 approach.

23 MS. HOLIDAY: Dr. Zanzonico and Dr.
24 Metter, NRC does not object to, if you want to amend
25 the subcommittee report to reflect these dual

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1 recommendations, that's at your discretion.

2 MEMBER METTER: Thank you, Sophie. I
3 think if that's okay, we'll go ahead. Any other
4 comments from the subcommittee? Because I think
5 we'll go ahead and make those two recommendations as
6 far as listing on the table as Dr. Zanzonico had
7 reflected.

8 MEMBER WEIL: This is Laura Weil. Dr.
9 Metter, may I comment on that?

10 MEMBER METTER: Yes.

11 MEMBER WEIL: I have no objection to
12 listing both sets of recommendations, but I would
13 like to know that they would be labeled with the
14 agency that recommends both the 100 and the 500
15 millisieverts threshold.

16 MEMBER METTER: Okay.

17 MEMBER WEIL: So that the chart or the
18 graph itself is labeled to indicate which agencies
19 recommend which threshold.

20 MEMBER METTER: Okay. I believe most of
21 them are based on the 100 millirem.

22 MEMBER WEIL: I believe that's true, and
23 I'd like to see that noted in the table.

24 MEMBER METTER: Oh, I see. Okay. Thank
25 you.

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1 Any other comments?

2 OPERATOR: And I am currently showing no
3 further questions or comments from the phones.
4 Again, as a reminder, if you have further questions
5 or comments, it is star one. Make sure your phone is
6 unmuted and record your name. And it is star two to
7 withdraw that request. And I'll stand by for any
8 further questions or comments at this time.

9 MEMBER METTER: Dr. Alderson, I don't
10 think there are other comments or questions at this
11 time.

12 CHAIRMAN ALDERSON: All right. Thank you
13 very much.

14 OPERATOR: And we did just have one cue
15 up. If you'd like to wait one moment, I'll get that
16 party's name.

17 CHAIRMAN ALDERSON: Certainly.

18 OPERATOR: One moment. Thank you. Excuse
19 me. Dr. Greenspan, your line is open for your
20 question or comment.

21 DR. GREENSPAN: Thank you very much. I
22 just had a quick comment as a follow up to
23 Dr. Zanzonico's request for references for gamma ray
24 constants. I'm traveling this week, but I will be
25 glad to provide them next week. I hope that won't be

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1 too late. Thank you.

2 VICE CHAIRMAN ZANZONICO: This is Pat
3 Zanzonico. Yes, Dr. Greenspan, that would be
4 certainly soon enough. The additional analyses I'm
5 committing to are going to take a bit of time, and
6 they certainly won't be concluded by next week, so
7 next week will be soon enough.

8 DR. GREENSPAN: Thank you very much.

9 OPERATOR: Thank you. And I'm currently
10 showing no further questions or comments at this
11 time.

12 CHAIRMAN ALDERSON: Good. Thank you.
13 That means that we will now proceed with the next
14 part of this public conference call. That will be
15 the report from Dr. John Suh's subcommittee on the
16 physical presence requirements for the Gamma Knife
17 Icon. I will turn the conversation over to Dr. Suh.

18 MS. HOLIDAY: Dr. Alderson and Dr. Suh,
19 before you launch into the next topic, if I may, can
20 I ask if the Committee will be making a motion to
21 endorse this report with the reflected amendments?

22 CHAIRMAN ALDERSON: Yes, certainly.
23 That's fine. Let's do that.

24 MEMBER METTER: Can I make a motion to
25 endorse the amended reports?

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1 PARTICIPANT: Second.

2 MS. HOLIDAY: And then if you could state
3 for me what the amendments will be, so that we can
4 capture that on the record?

5 MEMBER METTER: Okay. Dr. Zanzonico?

6 VICE CHAIRMAN ZANZONICO: Yes. The
7 amendments will include acknowledgment of the
8 benefits of breastfeeding. They will include
9 correction as needed of the specific gamma ray
10 constant values. They will include conversion of the
11 system of units from conventional to SI. There will
12 be an expanded dosimetric analysis of radioiodines as
13 a function of the age and thyroid mass of the child,
14 and also include other medical radionuclides --
15 radioisotopes of iodine.

16 We will include at least two additional
17 references as cited by Drs. Marcus and Sabin. And we
18 will include recommendations or recommended cessation
19 periods of time based on both a 100 and a 500 millirem
20 effective dose to the nursing child.

21 MS. HOLIDAY: Okay. Thank you, Dr.
22 Zanzonico.

23 CHAIRMAN ALDERSON: This is Dr. Alderson.
24 I think we should just mention that the transcription
25 errors/typos also will be corrected as recommended.

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1 MS. HOLIDAY: Thank you. Okay. Dr.
2 Alderson, now that there is a motion, can you call
3 for the vote?

4 CHAIRMAN ALDERSON: All right. All in
5 favor?

6 (Chorus of ayes.)

7 CHAIRMAN ALDERSON: Any opposed? (pause)
8 Hearing none, that passes unanimously.

9 CHAIRMAN ALDERSON: All right. So as I
10 stated a moment ago, I'll repeat now, it is now time
11 for us to consider the report on the physical presence
12 requirements for the Gamma Knife Icon, that
13 subcommittee report. That subcommittee is led by
14 Dr. John Suh. Dr. Suh, you're on.

15 MEMBER SUH: Okay. Thank you, Dr.
16 Alderson. I want to first thank the subcommittee
17 members, Dr. Ron Ennis and Laura Weil, and also thank
18 Sophie Holiday for her staff resource support.

19 So I will -- the charge to the subcommittee
20 was to propose the appropriate physical presence
21 requirements for Leksell Gamma Knife® Icon™
22 radiosurgery units. And I just want to go through
23 just a little bit about the gamma knife. The gamma
24 knife is a very well-established treatment for
25 patients with various benign and malignant brain

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1 tumors, vascular malformations, and functional
2 disorders, including trigeminal neuralgia.

3 The first gamma knife in the United States
4 was installed at the University of Pittsburgh in
5 1987, and over the years the gamma knife has evolved
6 and in 2006 the Perfexion™ unit was introduced, which
7 allowed for the authorized users to be inside the
8 treatment unit.

9 And given the differences between the
10 Perfexion™ versus the models U, B, and C, the
11 Perfexion™ was licensed under 10 CFR 35.1000. And as
12 of the reports, based on information collected, there
13 are 77 Perfexion™ units and 22 Icon™ units in the
14 United States, and worldwide over a million patients
15 have been treated with the gamma knife.

16 In terms of the current physical presence
17 requirements in 10 CFR part 35, it requires an
18 authorized user with appropriate training and
19 experience in radiation oncology and an authorized
20 medical physicist to be physically present throughout
21 all treatments involving the unit. And physical
22 presence has undergone some evolution. Initially, it
23 was defined as within hearing distance of normal
24 voice, and as part of a regulatory issue summary it
25 was further defined to be speaking in a normal

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1 conversational tone, not a raised voice. And they
2 made a comment that a distance of 20 feet may not be
3 close enough to adequately hear and respond to an
4 emergent situation.

5 The rationale for changing the physical
6 presence requirements is that the gamma knife unit,
7 as I mentioned, has evolved through the years. It is
8 important that any change we make allow the
9 authorized user to address an emergent situation and
10 also to verify that a correct dose was delivered.

11 If you look at the past 10 years of the
12 NMED report, there have been 10 reportable events
13 involving the Perfexion™, and only a minority of these
14 events occurred during a treatment.

15 So from the Perfexion™ there has been an
16 evolution to a newer unit called the Icon™ system.
17 Some of the fundamental differences with the Icon™
18 system is that it does allow for the option of a
19 thermoplastic frameless mask rather than a frame.
20 The majority of centers using the Icon™ system still
21 use a frame-based system rather than a mask-based
22 system. It does give the option for those patients
23 who may benefit from some type of fractionated
24 approach.

25 Number two is it allows the ability to

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1 perform integrated stereotactic cone beam CT, which
2 provides stereotactic reference for patient setups.

3 And number three is it also has a high
4 definition motion management for mask-based
5 treatments, which allows us to confirm that the
6 treatment is being delivered to the target itself.

7 There was a proposal from Elekta on
8 April 26th about the Gamma Knife® Icon™, and their
9 proposal is that an authorized user and authorized
10 medical physicist be physically present during the
11 initiation of all treatment involving a unit.

12 Number two is to have an authorized medical
13 physicist present throughout all patient treatments.

14 And number three is that an authorized user
15 physically be present in the department during
16 patient treatment and immediately be able to come to
17 the treatment room in case of emergency.

18 Based on the -- looking at the current
19 physical presence requirements, the evolution of the
20 Icon unit, the recommendations from the subcommittee
21 are that the authorized user and authorized medical
22 physicist be physically present during the initiation
23 of all treatments involving the Icon™, and that the
24 authorized medical physicist be physically present
25 throughout all treatments of the unit itself.

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1 We have made a recommendation that the
2 current physical presence requirements for the
3 authorized user be modified to allow the authorized
4 user to be close enough to the console area to respond
5 quickly to any issues that may arise.

6 The definition we came up with is that
7 within a two-minute walk of the Icon console area and
8 immediately available to come to the treatment room.
9 So it is very important that with this definition of
10 physical presence, the authorized user cannot be
11 involved in another procedure that would prevent him
12 or her to come immediately to the gamma knife in case
13 of an emergency.

14 In addition, we felt that it was important
15 that we do not use the definition of a department ,
16 as "department" can have different meanings to
17 different centers. So one could be stated that it's
18 part of a department, but the department could be
19 physically a long walk away. So we felt that there
20 should be some time restraint in terms of what
21 constitutes being physical present in terms of this
22 newer definition.

23 If there is an interruption of treatment
24 secondary to a medical or mechanical event, the
25 authorized user must return to the Gamma Knife® Icon™

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1 console area to evaluate patient and to review any of
2 the medical -- mechanical issues along with the
3 medical physicist.

4 And at the conclusion of treatment, the
5 authorized user must be present at the Icon console
6 to discuss any treatment or patient issues with the
7 patient, physicist, and a nurse.

8 The subcommittee felt that with these
9 modifications, in terms of current physical presence
10 requirements, it would allow more flexibility to the
11 authorized user.

12 In closing, we felt that it was very
13 important that the committee report did not encroach
14 on the practice of medicine, also allowed for the
15 regulator to inspect the regulated gamma knife
16 center, and also be consistent with regulations
17 governing a physician's supervision.

18 Any change that occurs to the current
19 physical presence requirements should take into
20 account that the culture of safety quality be
21 supported, given the superb track record for quality
22 and safety with the gamma knife.

23 Thank you. That concludes my report, Dr.
24 Alderson.

25 CHAIRMAN ALDERSON: All right. Thank you.

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1 Are there comments?

2 MEMBER SHEETZ: John, this is Mike Sheetz.
3 I have some comments.

4 CHAIRMAN ALDERSON: Please.

5 MEMBER SHEETZ: I think the subcommittee
6 provided an excellent report and overview of the
7 technological advances in gamma knife treatment since
8 the process has become more efficient allowing for
9 more treatments, and multiple targets can be treated
10 in a single session.

11 And they pointed out, based on the small
12 number of medical events involving modern gamma knife
13 models, it is, therefore, appropriate to evaluate the
14 required physical presence requirements for gamma
15 knife to see if they should be revised.

16 Based on our experience here at the
17 University of Pittsburgh where we have had every
18 model of the gamma knife, and we were the first to
19 license the U model in 1987, I have some comments
20 with respect to the recommendations of the
21 subcommittee, if I may proceed with those.

22 CHAIRMAN ALDERSON: Please.

23 MEMBER SHEETZ: I agree with the
24 recommendation number one that the AU and AMP need to
25 be physically present at the initiation of all

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1 treatments.

2 With respect to recommendation two, I think
3 the definition of "within a two-minute walk from a
4 gamma knife treatment console" will create ambiguity
5 for the regulatory compliance with licensees, and the
6 recommendation for the appropriately trained staff to
7 be present to respond to patient medical issues is
8 not really enforceable by the NRC.

9 So I would suggest consideration of this
10 recommendation to be modified to something that
11 actually is in current regulation for HDR right after
12 the initiation of treatment, an authorized medical
13 physicist and either an authorized user or a
14 physician under the supervision of an authorized user
15 who has been trained in the operation of emergency
16 procedures for response of the unit, to be physically
17 present during continuation of all patient treatments
18 involving the unit.

19 So I'll throw that up for consideration.
20 Again, it would be consistent with the HDR
21 requirements, and it would eliminate any ambiguity in
22 response times, and it would assure that appropriate
23 personnel are present to respond to any patient
24 medical issues.

25 I agree with recommendation three that the

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1 AU must return to the gamma knife console for the
2 interruption of treatment secondary to medical or
3 mechanical issues.

4 With respect to recommendation four that
5 requires the AU to be present at the gamma knife
6 treatment console at the conclusion of the treatment
7 to discuss any treatment or patient issues, if the
8 patient treatment has been completed without any
9 issues, I question whether this would be necessary.
10 And if you have eliminated this requirement, it would
11 provide greater relief to the authorized user.

12 And then the last slide on this, if the
13 subcommittee report -- not specifically saying, but
14 implies some modified physical presence requirements
15 should only be applicable to the Icon™ unit when using
16 the thermoplastic mask for patient treatment and not
17 the stereotactic beam, while the Icon™ utilizes an
18 integrated cone beam CT for stereotactic reference
19 and high-definition motion management systems, these
20 features are only required when using mask-based
21 treatments. They are not required for frame-based
22 treatments.

23 In our experience, less than 10 percent of
24 the gamma knife patient cases qualify for mask-based
25 treatments. There have been an extremely low number

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1 of medical events with Perfexion™ that have been
2 pointed out involving thousands of patient treatments
3 demonstrating a highly reliable treatment technology.

4 And so when using the Icon for frame-based
5 treatments, it is identical to the Perfexion™ unit
6 for frame based. So, therefore, I would suggest that
7 the revised physical presence requirements should
8 also be applicable to frame-based treatments on
9 either the Icon or the Perfexion™.

10 And that concludes my comments.

11 CHAIRMAN ALDERSON: Thank you. Dr. Suh?

12 MEMBER SUH: Thank you, Michael, for those
13 very thoughtful comments. So in terms of your second
14 recommendation about whether or not to support the
15 physical presence requirement of the two-minute walk,
16 this is something that the subcommittee grappled with
17 in terms of what would constitute appropriate
18 physical presence requirements with the Gamma Knife®
19 Icon™, and the number we came up with -- initially,
20 there was some discussion about whether or not being
21 physically present in the department would be
22 adequate, and we all agreed that that is too -- that
23 is too ambiguous. So we felt that was not a good
24 starting point.

25 And we grappled at the time -- we needed

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1 some type of time standpoint. And I do agree with
2 you that there could be some ambiguity in terms of
3 regulatory compliance. I actually have looked at
4 your comments. I actually thought about it.

5 And thinking about the HDR model, the
6 current proposal of either an authorized user or a
7 physician under the supervision of an authorized user
8 who has been trained in the operation of emergency
9 response to the unit be physically present during the
10 continuation of all patient treatments involving the
11 unit is a better definition, in my opinion, because
12 it then allows a physician to be present at the
13 console area or within voice distance during the
14 entire treatment.

15 As you mentioned, the NRC does not regulate
16 the ancillary staff such as nursing support, so that
17 is a consideration that I am certainly open to. I
18 would be curious to see what the other subcommittee
19 members think and also the rest of the committee as
20 well on that particular point.

21 In terms of the authorized user returning,
22 I'm glad that you agree with that comment. I do think
23 it's important for the authorized user to return.

24 In terms of recommendation number four, I
25 am probably not as strong an advocate for that. I do

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1 believe that the gamma knife does require an
2 authorized user to know what happened during the
3 treatment, and one of my concerns is that if the
4 authorized user does not know about the patient --
5 because, again, there could be a situation where the
6 treatment is "completed," but things may not have
7 gone as planned. And I think this is an opportunity
8 for the authorized user to deal with the medical
9 physicist to ensure everything has occurred
10 correctly.

11 Also, from a patient care standpoint,
12 having the authorized user there to let the patient
13 know that everything went well I think is a greater
14 assurance in terms of that the treatment actually did
15 go according to plan rather than having a surrogate
16 physician who has been trained to say, well,
17 treatment went well.

18 I have found that from a patient standpoint
19 it -- there is a better confidence when the physician
20 is actually there, the one who is actually involved
21 with the actual treatment.

22 In terms of number five, in terms of
23 whether or not the Icon™ and the Perfexion™ are
24 similar units, although the fundamental makings of
25 the Icon™ are very similar to the Perfexion™ unit,

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1 there is the opportunity to use a cone beam CT device
2 for the frame-based treatments.

3 What I can share with you is that at our
4 institution about 20 percent of our patients are
5 undergoing frame-based treatments right now,
6 typically up to five treatments sessions. And for
7 our functional cases and for those cases that we --
8 we have actually started to use the cone beam CT to
9 ensure that the alignment of what we saw on the
10 computer screen aligns with the frame attached to the
11 treatment machine.

12 So I don't feel that the Perfexion™ and the
13 Icon™ are similar. So I am not in support of modifying
14 physical presence requirements for both Perfexion™
15 and Icon™. I would propose that we change the
16 physical presence requirements for just the Icon™ unit
17 itself.

18 MEMBER ENNIS: This is Ron. Just to follow
19 up, being on the subcommittee, my thoughts to Mr.
20 Sheetz's comments. So in terms of the ambiguity of
21 the two-minute walk, well, certainly, there is a
22 little bit of ambiguity with that, although I don't
23 think it will be a lot because it does specify a time
24 which you can measure and walk. And of course people
25 can walk slightly faster or slower, but I don't think

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1 it's tremendously ambiguous.

2 So I'm comfortable with that. The notion
3 of instead requiring another physician to be there
4 under the supervision, I would be comfortable with
5 that, too. That is more restrictive on our users, I
6 think, than the proposed definition that our
7 subcommittee came up with.

8 And I think part of our charge was to see
9 whether we could provide safe relief to the
10 authorized user. So I don't know that our
11 constituents, if you will, or the people asking for
12 some relief would feel that we have provided any
13 relief with that. We could maybe hear what those
14 constituents had to say.

15 But I am comfortable with either, but I do
16 feel like what is written in the subcommittee report
17 is kind of aligned with providing some level of relief
18 while still being, you know, conservative in terms of
19 patient safety.

20 In terms of the other issues, the return at
21 the end I feel is an important component to this as
22 well. In my mind, it's kind of akin at the end of a
23 brachy procedure, kind of -- although we're not
24 requiring formal documentation, that the authorized
25 user documents that everything went as planned, or,

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1 if not, what kind of changes.

2 I do feel like it's really important to
3 close that loop. More subtle things that aren't quite
4 events might not be raised or you might forget about
5 them an hour later when you see each other in the
6 hall. But at that moment, the physicist and/or the
7 nurse or whoever might be there might be able to share
8 some issue about slight patient movement or things
9 like that that could be safety concerns that I think
10 will be lost if there is not that closure at the end.

11 In terms of the nurse issue, and whether
12 it's appropriate for these guidelines or not, I can
13 kind of certainly see the perspective that it's not
14 something NRC can regulate or does regulate, so it's
15 not appropriate for our subcommittee report. On the
16 other hand, it seems like a good practice advice.

17 I don't have a good sense of whether good
18 practice advice like this is appropriate or not. I
19 would turn to NRC staff for their comments on that.
20 It feels like a good idea to me, but I do get the
21 argument that it's a little bit more medical than
22 regulatory.

23 And on the final point of Perfexion™ versus
24 Icon™, frankly, I would defer to Dr. Suh's judgment.
25 He has a lot more experience with these units than I.

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1 So I don't have any particular opinion beyond his on
2 that.

3 I think I covered all the points. But if
4 there is something else, Mr. Sheetz, please remind
5 me.

6 MEMBER SHEETZ: This is Mike Sheetz. Thank
7 you for your consideration and responding to those -
8 - all of my comments.

9 So I guess, for clarity, you are
10 recommending these revisions for the Icon™ unit for
11 both frame-based and mask-based treatments. Is that
12 correct?

13 MEMBER ENNIS: That is correct. Yes.

14 MEMBER SHEETZ: Okay. The other comment is
15 we -- we do use the cone beam CT with frame based as
16 a replacement for the MRI or co-registration. But
17 otherwise, if we have a frame and an MRI image, we
18 would not repeat the cone beam CT, you know, as a
19 secondary check. And I'm not sure that's standard.

20 So, again, I guess I still go back to frame-
21 based treatments on Icon™ and Perfexion™ are identical
22 in practice.

23 MR. OUHIB: Hi. This is Zoubir.

24 CHAIRMAN ALDERSON: Go ahead.

25 MR. OUHIB: On item number two, you know,

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1 trying to use the HDR regulation type of thing, I
2 think it's a good idea. However, there are
3 institutions that might not be as fortunate to have
4 the luxury of a physician under the direct
5 supervision of an authorized user.

6 So perhaps consideration would be to use
7 one or the other; in other words, to keep the two-
8 minute option and perhaps -- or the presence of a
9 physician under the direct supervision of an
10 authorized user.

11 CHAIRMAN ALDERSON: Are there further
12 comments? Is there anyone that would like to comment
13 on that statement?

14 MEMBER SUH: This is John Suh. So I can
15 see both points. So in terms of being less
16 restrictive, the two-minute walk from a gamma knife
17 treatment console area is certainly less restrictive.
18 Again, as Ron mentioned, you know, one can walk faster
19 or slower, but, again, I think if someone says two
20 minutes, that's something that the authorized user
21 could work with in terms of what is considered a two-
22 minute walk. Physicians would need to decide what
23 constitutes that as a safety parameter.

24 You know, in terms of this proposal of
25 either an authorized user or physician under the

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1 supervision of authorized user be present, it does -
2 - it's probably a clearer definition, although it is
3 somewhat more restrictive. And for a smaller center
4 that may not have the luxury of having another
5 physician involved, I can see this being a more
6 restrictive definition for gamma knife.

7 Not all gamma knife centers have multiple
8 physicians who are: a) trained, and b) have an
9 interest in being involved in gamma knife.

10 In terms of doing both, I guess I have mixed
11 feelings about whether or not both is a good option.
12 I think we should stick with one option if we are
13 going to go ahead with changing the current physical
14 presence requirements, which was the charge of the
15 subcommittee to begin with.

16 CHAIRMAN ALDERSON: Further comments? I
17 think we still need to work to clarify this a bit.
18 I'm going to take the prerogative here to indicate
19 what I think is being said, and then I'd like to get,
20 John, your comments and that of the Committee to
21 clarify this.

22 So I am hearing that regarding the comment
23 of extending this new approach to both the Icon™ and
24 the Perfexion™, I believe that the Committee is saying
25 that it would choose to stay with the Icon™ alone,

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1 that there should be -- the physician should be
2 present at the end of the treatment, so that they can
3 talk to the patient.

4 Am I correct on the Committee's position on
5 those two issues?

6 MEMBER SUH: This is John Suh speaking
7 again. Yes, I do believe that the Icon™ and Perfexion™
8 are different units.

9 CHAIRMAN ALDERSON: Yes.

10 MEMBER SUH: And your second point about
11 being present at the conclusion of treatment, like
12 Ron, I feel very strongly that it is important to
13 close the loop when treating patients with high
14 dose/high precision radiation that is offered with
15 the Icon™ Gamma Knife® unit.

16 CHAIRMAN ALDERSON: Right. Am I correct
17 that Dr. Ennis and Laura Weil agree with those
18 positions?

19 MEMBER ENNIS: This is Ron. So just to
20 clarify, on the second position of being there at the
21 end, I agree with the position. But to clarify the
22 rationale, for me, it's not just about the patient -
23 - you know, good for the patient, the patient will
24 like that, and all that, which I totally agree, but
25 that's really a medical thing.

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1 But I do feel like there could be more
2 subtle or minor safety concerns, issues that might
3 have happened that would not stop the treatment and
4 would not be a misadministration, but might be
5 helpful for the team to know going forward for the
6 next case or the next patient, where things weren't
7 perfect, that it's really important to have that kind
8 of -- well, they call it a huddle nowadays, right?
9 Doing essentially a mandated huddle from a safety
10 point of view at the end of treatment, which will
11 only really happen efficiently and effectively, in my
12 opinion, if we mandate that everyone gets together at
13 the end.

14 CHAIRMAN ALDERSON: Yes. Good. Any
15 disagreement with that from Dr. Suh or Ms. Weil?

16 MEMBER WEIL: No.

17 MEMBER SUH: No.

18 CHAIRMAN ALDERSON: Okay. So I think that
19 we have resolved those two issues in terms of the
20 committee's response to the comments. And that
21 leaves us with the comment regarding the two-minute
22 walk versus someone, being the AU or an AU-trained
23 person, being physically present at all times.

24 I'm going to turn this back to Dr. Suh to
25 try to see if we can navigate our way through that

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1 particular concern, which seems to be the significant
2 one remaining in this discussion.

3 MEMBER SUH: So I have been thinking about
4 this since, you know, Michael sent this to me. As I
5 said, I am -- I like his suggestion, but I do agree
6 that it is more restrictive. And, again, it should
7 be very apparent. You know, a two-minute walk I don't
8 think should be that ambiguous in terms of responding
9 to an emergency or if there is an issue with a
10 patient.

11 But my personal feeling, my recommendation,
12 is that the subcommittee report of the altered
13 current physical presence to allow for the authorized
14 user to be within a two-minute walk of the gamma knife
15 console area is appropriate and will allow the
16 authorized user to respond to any immediate medical
17 needs.

18 CHAIRMAN ALDERSON: Okay. Good. That's
19 definitive. Do Dr. Ennis and Ms. Weil agree?

20 MEMBER ENNIS: I do.

21 CHAIRMAN ALDERSON: Laura?

22 MEMBER WEIL: Yes, I do.

23 CHAIRMAN ALDERSON: Okay. So that's also
24 clear from the standpoint of the subcommittee. Are
25 there other comments before we open this up to people

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1 who might be on the phone lines?

2 So with the help of the operator, we will
3 now take comments on any of these issues from people
4 who are on the phone?

5 OPERATOR: Thank you. And, again, as a
6 reminder, if you have a question or a comment from
7 the phone, please press star one at this time. Make
8 sure your phone is unmuted and record your name to
9 introduce your question. And to withdraw that
10 request, you may press star two. Once again, for
11 questions or comments, press star one and record your
12 name at this time.

13 And one moment. We'll stand by for
14 questions or comments. One moment, please. And we
15 do have a question or comment from Susan Lohman. Your
16 line is open.

17 MS. LOHMAN: Thank you. This is Susan
18 Lohman. I am neuroscience applications manager with
19 Elekta. And, first, I'd like to thank the
20 subcommittee for their long and thorough review of
21 this issue, the process that they have gone through.

22 And at this time, I would like to urge the
23 subcommittee and Committee to move forward with the
24 subcommittee's recommendation as it was proposed and
25 possibly in the future come back to look at the

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1 inclusion or continued exclusion of Perfexion™.

2 And myself, as a representative of Elekta,
3 would be more than willing to provide any subject
4 material necessary to proceed as such.

5 Thank you.

6 CHAIRMAN ALDERSON: Do we have other
7 comments?

8 OPERATOR: Yes, we do have another question
9 or comment. And our next question or comment is from
10 Frank Tran. Your line is open.

11 MR. TRAN: Yes. This is Frank Tran in
12 Region III, NRC. I have a comment on the rule with
13 the HDR of exactly they -- they didn't require direct
14 supervision from an authorized user or a trained
15 person. It just says under supervision. So I believe
16 the key is not that. So I just want to comment on
17 that.

18 CHAIRMAN ALDERSON: This is Dr. Alderson.
19 I'd like to ask the commenter to repeat some of what
20 he said, because I don't know how other -- I didn't
21 actually hear all those words very clearly.

22 MR. TRAN: Okay. So earlier I believe that
23 Mike mentioned about the rule under -- that required
24 authorizer user to be -- or a trained person to be
25 present over the -- under the rule for the HDR.

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1 Another person mentioned that there should be direct
2 supervision.

3 However, under the rule for the HDR, it is
4 not a direct supervision, just a supervision, either
5 direct or not direct. So there's the comment for
6 that.

7 CHAIRMAN ALDERSON: All right. Did people
8 understand the comment?

9 PARTICIPANT: Yes.

10 CHAIRMAN ALDERSON: Okay. Are there
11 further comments?

12 OPERATOR: I am currently showing no
13 further questions or comments at this time. And,
14 again, as a reminder, that is star one. Make sure
15 your phone is unmuted and record your name. And it
16 is star two to withdraw that request.

17 Again, for further questions or comments at
18 this time, please press star one and record your name,
19 and I'll stand by for further questions or comments.

20 CHAIRMAN ALDERSON: So, Dr. Suh, I'm going
21 to summarize here how I think this conversation has
22 evolved. I think we have listened to all of the
23 comments. We have made comments in return. I believe
24 that we're at the point where we are ready to accept
25 the proposal as it was originally recommended. Is

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1 that how you also understand the comments?

2 MEMBER SUH: Yes, Dr. Alderson.

3 CHAIRMAN ALDERSON: Okay. Well, in that
4 case, are we in fact ready to -- is the subcommittee
5 and the -- are the ACMUI members ready -- to accept
6 the report as it was originally proposed? All those
7 in favor?

8 (Chorus of ayes.)

9 CHAIRMAN ALDERSON: Any opposed? Thank
10 you. This report is accepted in its original proposed
11 form.

12 MS. HOLIDAY: Dr. Alderson, if I may, I'm
13 sorry, I didn't catch who made the motion and who
14 seconded the motion.

15 CHAIRMAN ALDERSON: I believe it was
16 implied that Dr. Suh was making the recommendation,
17 I believe.

18 MEMBER SUH: Yes. On behalf of the
19 subcommittee, I propose that we accept the current -
20 - sorry, the physical presence requirements of the
21 Leksell Gamma Knife® Icon™ as submitted on behalf of
22 the subcommittee members.

23 VICE CHAIRMAN ZANZONICO: Sophie, this is
24 Pat. I'll second it.

25 MS. HOLIDAY: Thank you.

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1 CHAIRMAN ALDERSON: Good.

2 MS. HOLIDAY: And then, if I understand,
3 was this a unanimous endorsement, or were there any
4 dissentions or abstentions?

5 CHAIRMAN ALDERSON: I did ask for that, I
6 believe, and it is a unanimous endorsement.

7 MS. HOLIDAY: Okay. Thank you.

8 CHAIRMAN ALDERSON: So is there any other
9 business that we need to conduct this morning?

10 MS. HOLIDAY: No. I would just like to
11 thank the subcommittee members for putting forth all
12 of the effort for both Dr. Metter's subcommittee and
13 Dr. Suh's subcommittee, for their thorough reviews
14 and their reports. I would also like to remind the
15 ACMUI members and other participants on the phone
16 that ACMUI will be holding another public
17 teleconference in two weeks on March 1st from
18 2:00 p.m. to 4:00 p.m. eastern.

19 The topic of that teleconference will be
20 the subcommittee report for the training and
21 experience requirements under all modalities in
22 10 CFR part 35 with a focus on 35.300 uses.

23 The ACMUI will also be holding their spring
24 meeting here at NRC headquarters on March 7th and
25 8th.

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1 Thank you.

2 CHAIRMAN ALDERSON: Well, thank for
3 everyone who was on the call today.

4 Mr. Bollock, anything you would like to say
5 in the end?

6 MR. BOLLOCK: No, thank you, Dr. Alderson.
7 Appreciate everyone's time.

8 CHAIRMAN ALDERSON: I believe, Sophie, that
9 we have concluded our business. Thank you all,
10 everyone.

11 (Whereupon, the discussion of the draft
12 report concluded at 10:19 a.m.)

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February 7, 2018

Advisory Committee on Medical Uses of Isotopes (ACMUI)
U.S. Nuclear Regulatory Commission
11555 Rockville Pike
Rockville, MD 20852

c/o Ms. Sophie Holiday, Sophie.Holiday@nrc.gov

Dear Ms. Holiday and Members of the ACMUI:

We have reviewed the ACMUI subcommittee draft on Nursing Mother Guidelines for the Medical Administration of Radioactive Materials, which is to be discussed at the Feb. 15, 2018 ACMUI meeting. We have a number of comments which we believe should be addressed in the next draft of this document which should make the final document more useful.

1. The draft guidance document assumes theoretical risk to the infant but fails to include information on the benefits of breastfeeding, which are real and significant. According to the American Academy of Pediatrics (AAP):

“Most health professionals are familiar with the benefits of breastfeeding. The AAP continues to support the unequivocal evidence that breastfeeding protects against a variety of diseases and conditions in the infant such as: bacteremia, diarrhea, respiratory tract infection, necrotizing enterocolitis, otitis media, urinary tract infection, late-onset sepsis in preterm infants, type 1 and type 2 diabetes, lymphoma, leukemia, and Hodgkins’ disease, childhood overweight and obesity. There are also maternal health benefits to breastfeeding such as: decreased postpartum bleeding and more rapid uterine involution, decreased menstrual blood loss and increased child spacing (lactational amenorrhea), earlier return to prepregnancy weight, decreased risk of breast and ovarian cancers.”

2. We note that the specific gamma ray factors cited in Table 2 are incorrect, by a factor of 1000(!) We hope that this is an error in the table, and that erroneous gamma factors were not used in the calculations given in the document.
3. We note a number of typos that suggest that the document was not carefully reviewed:
 - a. In Table 5, the heading "Hazel and Breitz" should be "Stabin and Breitz". "Hazel" is Breitz's first name.
 - b. The reference 'Stabin and Breitz' is repeated as references 10, 26, 31, 36, 54, 71, and 73.
 - c. The proper spelling of Lu is "lutetium", not "lutecium", but this is misspelled several times in the document.
 - d. The word 'radioisotope' is substituted for 'radionuclide' twice. 'Radionuclide' is the general term for a radioactive species; 'isotope' refers to different radioactive species of a given element.
 - e. In all cases 'et al' should be 'et al.' (abbreviation mark included).
 - f. The name of the computer program is 'OLINDA/EXM'.
 - g. Page 8: 'generallyless' is given as one word.
 - h. Table 1 – do not capitalize 'rad'.
 - i. On page 4 last line and in Table 2 the half-life of F-18 is given as 1.2 hours. The half-life of F-18 is 110 minutes, or 1.83 hours.
 - j. It is odd that non-SI units are used preferentially in a 2018 document.
4. For ingestion of radioiodinated pharmaceuticals, the document should contain thyroid dosimetry for all radionuclides of iodine to the infant thyroid as a function of infant uptake and thyroid mass/infant age. Choosing the worst possible case of a newborn with extremely high uptake and a tiny thyroid gland is not useful once the uptake falls from 75%-100% to about 15% and the thyroid mass increases, so a whole range of values needs to be presented. This information is important not only when considering advice to the mother but in evaluating accidents as well, of which there have been a number over the years.
5. We were pleased to see the calculations for external dose to the infant using the mother as a line source instead of a point source. We have two issues, however, with the calculations:
 - a. The authors appear to be unaware of important literature on the subject, noting 'the general lack of pertinent data in the literature.' We note, for example:
 - i. J. G. Hunt, D. Nosske, D. S. dos Santos. Estimation of the dose to the nursing infant due to direct irradiation from activity present in maternal organs and tissues. Radiation Protection Dosimetry, Volume 113, Issue 3, 28 April 2005, Pages 290–299.
 - ii. Mountford PJ and Coakley AJ. Radiopharmaceuticals in breast milk. Proceedings, Fourth International Radiopharmaceutical Dosimetry Symposium, Oak Ridge Associated Universities, Oak Ridge, TN, 1986; 167-180.
 - b. In calculating external dose to the infant from the radioactive mother, humanized gamma ray constants should be used or estimated, as the specific gamma ray

constants significantly overestimate infant dose. For example, the humanized gamma ray constant for I-131, with a 364 keV photon, is 1.3, not 2.2 (RADAR Exposure and Dose Calculator, <http://www.doseinfo-radar.com/ExposureCalculator.html>). For radionuclides with lower photon energy, the humanized gamma ray constants would reflect even more self-absorption by the mother. In the case of a mother with thyroid cancer who has stopped breastfeeding entirely and who has no thyroid of her own (it has been surgically removed), an accurate external dose to the infant after a 5 mCi administration for a metastatic survey and after a 150 mCi administration of a therapy dose should be calculated and appear in this guidance document, so the physician can offer accurate advice about holding the infant and feeding him formula or other milk product.

6. We appreciate that 10CFR35.75 notes a dose limit of 5 mSv (500 mrem) for exposure to members of the public, but requires that guidance be given regarding interruption of breast feeding if the dose to an infant or child may exceed 1 mSv (100 mrem). *We strongly suggest that this second requirement be changed (in the statute) to 5 mSv, and the calculations be redone.* The calculations performed were already conservative, but the application of an additional factor of 5 has no scientific basis. There are no scientifically valid data showing harm to infants at a dose of 500 mrem, and it is therefore unreasonable to reduce the dose far below the legal limit. Every baby conceived and born in Denver, CO has received an extra 500 mrem from background radiation by the age of 15 months, over and above the United States average which is 300 mrem/y. (Background radiation in Denver is about 550 mrem/y). Year after year, the State of Colorado tends to be tied for the third lowest cancer death rate in America, despite the fact that residents receive an extra 250 mrem/y, every year. Some receive even higher doses (Copper City, CO has a background rate of about 890 mrem/y.). By clinging to the Linear No-Threshold (LNT) myth that says any amount of radiation is dangerous and can cause death from cancer, 500 mrem seems five times more dangerous than 100 mrem, but the LNT premise itself has been soundly denounced on various fronts for low dose and dose rates. First, the LNT states that there is no such thing as radiation repair, but we have found over 150 genes that are active in the repair of lesions caused by radiation and metabolism using oxygen, and we know that these repair mechanisms are stimulated by low dose radiation and that they repair more damage than what was caused by the low dose radiation to begin with. We know that one mutation cannot cause a cancer, fatal or otherwise, as assumed by the LNT. If it could, we would see three-year old boys with prostate cancer, five-year old boys and girls with breast cancer, and six-year olds with lung cancer. This does not happen. The LNT states that all doses are additive, and that dose rate is irrelevant. We know that radiation delivered chronically in low doses is much less damaging than the same dose delivered instantaneously. The whole field of radiation oncology is mainly based on the fact that normal tissues can repair if the radiation doses delivered are not too high and repair mechanisms are stimulated, whereas aberrant cancer tissue cannot repair as well as normal tissue. That is why radiation therapy is delivered multiple times over weeks, permitting normal tissue to preferentially repair. If 6000 rad were delivered all at once, you would burn a hole in the patient. It is time to stop using the LNT at low doses as a basis for anything.

Thank you for your attention and consideration. We look forward to reviewing the improved draft.

Sincerely,

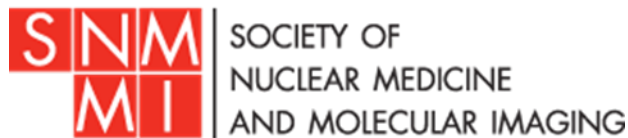


Carol S. Marcus, Ph.D., M.D.

Professor of Radiation Oncology, of Molecular and Medical Pharmacology (Nuclear Medicine), and of Radiological Sciences, David Geffen School of Medicine at the University of California at Los Angeles (UCLA) and past two-term member of the ACMUI.



Michael G. Stabin
Chair, RAdiation Dose Assessment Resource (RADAR) Committee of the Society of Nuclear
Medicine and Molecular Imaging, and
Associate Professor of Radiology and Radiological Sciences
Department of Radiology and Radiological Sciences
Vanderbilt University



February 12, 2018

U.S. Nuclear Regulatory Commission (NRC)
11555 Rockville Pike
Rockville, MD 20852
Washington, DC 20555-0001

Re: Nursing Mother Guidelines for the Medical Administration of Radioactive Materials

Dear members of the ACMUI:

The Society of Nuclear Medicine and Molecular Imaging (SNMMI) appreciates the opportunity to comment on the Sub-Committee on Nursing Mother Guidelines for the Medical Administration of Radioactive Materials report drafted by Vasken Dilsizian, MD, Darlene Metter, MD (Chair), Christopher Palestro, MD, and Pat Zanzonico, Ph.D, dated February 1, 2018.

The Society of Nuclear Medicine and Molecular Imaging's more than 17,000 members set the standard for molecular imaging and nuclear medicine practice by creating guidelines, sharing information through journals and meetings, and leading advocacy on key issues that affect molecular imaging and therapy research and practice.

SNMMI has reviewed the draft on Nursing Mother Guidelines for the Medical Administration of Radioactive Materials. We believe this is an excellent first draft, however, there are some few errors that should be corrected.

First, while not an error, the benefits of breastfeeding to the infant and to the mother should be mentioned.

Specific gamma ray constants are markedly incorrect, and should be:

- F-18: 6.952E-4 mrem/hr per uCi at 1 m
- Ga-67: 1.1 x 10⁻¹ mR/hr/mCi at 1 m
- Tc-99m: 1.2 x 10⁻¹ mrem/hr/mCi at 1 m
- I-131: 2.2 R-cm²/mCi-hr

Page 8, line 1, "generallyless" should be two words.

Page 11, #6 (and possibly elsewhere), "lutecium" is correctly spelled "lutetium".

Table 1, "Rad" should be "rad"

Table 2 half life of F-18 is 109 or 110 minutes (depending on the reference, and is therefore 1.82 or 1.83 hours (not 1.2). This is also mentioned incorrectly in the last line of page 4.

Table 5, 3rd column, the reference should be Stabin and Breitz.
References 10, 26, 31, 36, 54, 71 and 73 are all the same reference (Stabin and Breitz).

Additionally, the report offers some debatable recommendations. For example, interrupting breast feeding for 7 days for I-123 400 microcurie capsules. That is significantly longer than 10 half-lives (even though the risk of contamination with other isotopes is no longer present - the previous rationale for interrupting breast feeding). Also, most sources say no interruption of breast feeding is necessary including the NRC regulatory guide 8.39 <https://www.nrc.gov/docs/ML0833/ML083300045.pdf> (no cessation needed even for doses of 3 mCi) https://www.nrc.gov/materials/miau/miau-reg-initiatives/guide_2002.pdf.

There are certain assumptions of the LNT hypothesis that are lacking in supportive scientific evidence. For one, LNT assumes that there is no DNA repair at low doses. However, the scientific evidence suggests otherwise. There have been over 150 genes identified by radiation biologists that are involved in the repair of DNA radiation damage. There are known to be three types of repair:

- 1) anti-oxidant prevention
- 2) enzymatic repair of DNA damage
- 3) removal of DNA alterations by apoptosis.

Another assumption of the LNT that needs to be addressed is that the dose rate does not matter. However, that supposition is also not supported by scientific evidence. In fact, the entire field of Radiation Oncology is based on repair of radiation damage, and particularly that the repair mechanisms of normal tissue are more efficient than those of cancerous tissue.

SNMMI appreciates the opportunity to comment on this report. As always, SNMMI is ready to discuss any of its comments or meet with NRC on the above issues. In this regard, please contact Caitlin Kubler, Senior Manager, Regulatory Affairs, by email at ckubler@snmmi.org or by phone at 703-326-1190.

Sincerely,

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