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UNITED STATES OF AMERICA

NUCLEAR REGULATORY COMMISSION

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ADVISORY COMMITTEE ON THE MEDICAL USES OF ISOTOPES

+ + + + +

TELECONFERENCE

+ + + + +

THURSDAY, FEBRUARY 15, 2018

+ + + + +

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

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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

VERED SHAFFER, RES

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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
ASF AW 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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JERRY GEORGE, Baptist Health South Florida

KIMBERLY GILLIAM, VA Radioactive Materials
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THEODORE GODFREY, Elekta, Inc.

BENNETT GREENSPAN, Society of Nuclear Medicine
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CAROL MARCUS, University of California at Los
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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.

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Medical School

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LOU SHIMABUKU, *unaffiliated*

EUGENIO SILVERSTRINI, Northwell Health

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CINDY TOMLINSON, American Society of Radiation
Oncology (ASTRO)

MICHAEL WELLING, University of Virginia

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

2 (9:06 a.m.)

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

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

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

16 My name is Doug Bollock. I am the chief
17 of the Medical Safety and Events Assessment Branch,
18 and I have been designated as the federal officer for
19 this Advisory Committee in accordance with 10 CFR Part
20 7.11.

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

24 This announced meeting of the Committee is

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

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

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

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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 Ouhib?

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 selected
14 as the ACMUI nuclear pharmacist. And Ms. Shober has
15 been selected as the ACMUI Agreement State
16 Representative.

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

21 I now ask NRC staff members who are present
22 to identify themselves. I'll start with individuals
23 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 mute.
10 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 employees
17 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
24 H-O-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 access
3 the bridge line is 279-0867 followed by the pound key.

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

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

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

22 Comments and questions are usually
23 addressed by the Committee near the end of the
24 presentation after the Committee has fully discussed
25 the topic. We ask that one person speak at a time as

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1 this meeting is also closed caption.

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

5 At this time, I'd ask that everyone on the
6 call who is not speaking to place their phones on mute.

7 If you do not have the capability to mute your phone,
8 please press star six to utilize the conference line
9 mute and unmute function.

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

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

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

20 MEMBER METTER: Thank you, Dr. Alderson.

21 And I'd like to first thank the work of my subcommittee
22 members, Dr. Vasken Dilsizian, Dr. Christopher
23 Palestro, and Dr. Pat Zanzonico.

24 The subcommittee charge was to review the
25 radiation exposure from diagnostic and therapeutic

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1 radiopharmaceuticals, including brachytherapy, to the
2 nursing mother and child.

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

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

22 The subcommittee results and
23 recommendations are summarized in a table reviewed at
24 the September 2017 ACMUI meeting. Since that time,
25 there have been comments from Dr. Carol Marcus and Dr.

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1 Michael Stabin, and Dr. Bennett Greenspan and the SNMMI.

2 To review these comments, Dr. Pat Zanzonico will
3 address them and the associated report revisions.

4 Dr. Zanzonico?

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

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

20 And that point is well taken, and in our
21 subsequent revision of the report we think it would
22 be reasonable to include a statement explicitly
23 acknowledging the benefits of breastfeeding to the
24 mother and child, and so we plan to do that in the revised
25 -- the subsequent revision of our report.

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

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

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

19 And of course if we have numerical or other
20 factual errors in the report, those will be corrected
21 and reflected in a revised analysis. However, we asked
22 that Dr. Greenspan and the SNMMI provide a reference
23 for their values. No such reference was provided with
24 their written comments, and so we have no way at this
25 point of verifying their veracity, their accuracy.

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

9 And if Dr. Greenspan and the Society can
10 provide a reference, so that we can verify the accuracy
11 of their stated values, we will amend our report
12 accordingly.

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

21 One issue that arose, which is always a
22 thorny one, is the system of units to use. We use
23 essentially conventional units because, frankly,
24 that's the system of units most of us, including myself,
25 are most familiar with and most comfortable with. But

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1 we certainly appreciate that we should be transitioning
2 to use of SI units.

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

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

16 And Drs. Marcus and Stabin recommended that
17 we perform this thyroid dosimetry analysis for all
18 medically used radioiodines, not just I-131. So that
19 would include, of course, I-123, nowadays I-124,
20 perhaps even I-125. And they also suggested that in
21 that analysis we use a range of uptakes, not simply
22 maximal uptake, and a range of age-dependent uptakes
23 and age-dependent thyroid masses. And we can certainly
24 do that.

25 And, immodestly, I cite my own paper,

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1 Age-Dependent Thyroid-Absorbed Doses for
2 Radiobiologically Significant Radioisotopes of Iodine
3 from Health Physics, 2000. So we can extract dose
4 estimates or -- in the dosimetry analysis from that
5 paper and incorporate the suggested, augmented analysis
6 in the subsequent revision of our report.

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

16 And they also point out that perhaps an
17 ill-advised phrase was included in the report
18 referencing the available scientific literature on
19 breastfeeding, dosimetry, and so forth; namely, the
20 phrase being the general lack of pertinent data in the
21 literature. And on further reflection, I think we all
22 acknowledge -- and you can verify this by looking at
23 the bibliography -- the references in our report, there
24 actually is already significant literature on the
25 subject. So we will eliminate that phrase as well as

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1 include these additional references.

2 A further point that was made is that rather
3 than using or modeling the mother and the mother's breast
4 as point sources -- and that is often done, frankly,
5 for simplicity purposes in dose calculations -- we
6 modeled those source regions in terms of the external
7 dose to the nursing baby. We modeled those as line
8 sources based on a paper in the literature, and that
9 yields a more realistic estimate of the external dose
10 to the infant than does a point source model.

11 Drs. Marcus and Stabin point out, however,
12 that there are so-called humanized gamma ray constants
13 available, certainly at least for I-131. However, we
14 point out -- or we would like to point out that in our
15 calculation we not only model the mother's body and
16 breast as line sources, but we also incorporated the
17 self-absorption of extant gamma rays by those
18 respective source regions, and we also -- well, we
19 modeled those, as I say, as attempting to count the
20 self-absorption.

21 So we think that our approach, even though
22 we use specific gamma ray constants which implicitly
23 implies -- which implies a point source, we think we've
24 made the necessary adjustments to appropriately
25 quote/unquote "humanize our specific gamma ray constant

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1 values."

2 I'm just thumbing through my notes.
3 Another point that was made -- and this was a lengthy,
4 very scholarly comment, indicating that basing
5 recommendations with regard to cessation of
6 breastfeeding for mothers who undergo a nuclear
7 medicine procedure, basing that on a 100 millirem limit
8 to the nursing infant is overly conservative, and Drs.
9 Marcus and Stabin recommend a dose limit of five
10 millisieverts instead.

11 And incorporated into that comment was a
12 strong reputation of the linear non-threshold dose
13 response model for cancer induction by radiation. And
14 I think many of us, myself included, are very empathetic
15 so to speak to that point, and I think many of us have
16 well-founded skepticism about the biological validity
17 of the linear non-threshold model.

18 But having said that, really, a discussion
19 of that model, as important and interesting as it is
20 certainly, is really beyond the scope of our report.

21 And as Dr. Metter pointed out, we deferred to the
22 prevailing recommendations made by authoritative
23 bodies like the ICRP, NCRP, and so forth.

24 And we also noted that in their original
25 analysis, in the really seminal and widely cited paper

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1 by Dr. Stabin and Dr. Bryce, that they based their
2 analysis on a one millisievert effective dose
3 quote/unquote limit to the nursing infant.

4 So based on all of those considerations,
5 and despite our misgivings of the linear non-threshold
6 dose-response models, we decided, as Dr. Metter
7 indicated, to use a one millisievert limit upon which
8 to base our recommendations.

9 Proceeding now to the comments submitted
10 by Dr. Greenspan and the Society, to address their
11 comment on the possible -- possibly erroneous specific
12 gamma ray constant values, and we will ask them and
13 await the literature citation of the values they cite,
14 and based on our subsequent review of these values in
15 that literature adjust the specific gamma ray constants
16 and our values and our calculations accordingly.

17 I mentioned that they also had a number of
18 editorial corrections which we will certainly address
19 in a subsequent revision of the paper. And there was
20 a question or a disagreement with our recommendation
21 for discontinuing of breastfeeding following
22 administration of I-123 labeled radiopharmaceuticals,
23 not only sodium iodide but also ortho-iodohippurate
24 and MIGB, metaiodobenzylguanidine, which are all used
25 clinically labeled with I-123.

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1 And I think there may have been a
2 misunderstanding, understandably, given all of the
3 numbers and so forth in the paper, in the report rather,
4 but in Table 2 -- I'm sorry, in Table 5 of the report,
5 in which we include our recommendations on cessation,
6 the penultimate column, the next-to-last column, which
7 use the -- which list the current recommendations of
8 -- that we use here at Memorial Sloan Kettering,
9 indicated a seven-day discontinuation following
10 administration of at least certain I-123
11 radiopharmaceuticals.

12 But if you looked at the recommendations
13 for -- from the Committee, which is actually in the
14 very last column of that table, our recommendations
15 are much shorter, no more than 48 hours, and in the
16 case of I-123, iodohippurate, not recommending any
17 interruption of breastfeeding.

18 So I think we have all -- I think what we
19 -- what the committee or subcommittee has recommended
20 is perfectly consistent with the point that Dr.
21 Greenspan and the Society were making. So, yes, as
22 you see what's on the screen now, in the very last
23 column, the fourth, fifth, and sixth lines refer to
24 cessation of I-123, sodium iodide;
25 metaiodobenzylguanidine, MIGB; and the last of those

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1 three lines, line 6, to ortho-iodohippurate labeled
2 with I-123. So I think our recommendations are
3 consistent with what the Society is recommending.

4 Dr. Greenspan and the Society are also
5 recommending a more thorough, a more complete
6 dosimetric analysis of radioiodine as a function of
7 age, child age, and thyroid mass. And as I alluded
8 to earlier, we will provide an expanded dosimetric
9 analysis as also recommended by Drs. Marcus and Stabin.

10 And Dr. Greenspan and the Society also
11 forcefully endorsed the recommendation of Drs. Marcus
12 and Stabin that, number one, a 500 millirem rather than
13 a 100 millirem dose limit or dose benchmark upon which
14 to base recommendations is more appropriate, and that
15 the linear non-threshold model is really not only
16 inappropriate but incorrect.

17 So I have already addressed that point in
18 my earlier comments. And so that actually completes
19 our point-by-point response to the submitted comments,
20 both by Drs. Marcus and Stabin, and by Dr. Greenspan
21 and the Society. We very much appreciate their careful
22 and thoughtful -- their careful reading of the report
23 and their thoughtful comments. And we have tried to
24 address them as comprehensively as possible. And I
25 think we've done so and will revise the report

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1 accordingly.

2 So that concludes my comments in terms of
3 our responses to the submitted comments. So, Dr.
4 Metter, I will turn it back to you.

5 MEMBER METTER: Thank you, Dr. Zanzonico,
6 for a very thorough review and work on the comments
7 from Drs. Marcus, Stabin, Greenspan, and the Society
8 of Nuclear Medicine.

9 Do I have other comments from our
10 subcommittee members?

11 Okay. Hearing none --

12 MEMBER WEIL: Dr. Metter?

13 MEMBER METTER: Yes.

14 MEMBER WEIL: This is Laura Weil. I do
15 have a comment, and I'd like to apologize for not
16 submitting it in advance. The subcommittee report
17 recommends the complete cessation of -- states that
18 the cessation of milk production generally occurs about
19 six weeks after the last breastfeeding.

20 And I encountered a report from the APA,
21 which recommends a longer period of cessation, and I'd
22 like to -- this is from the ATA from 2009 in Thyroid.

23 If I might just briefly read this paragraph and ask
24 for an evaluation of it, basically.

25 Let's see. Breastfeeding must be stopped

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1 at least six weeks before administration of I-131
2 therapy, and a delay of three months will more reliably
3 ensure that lactation-associated increase in breast
4 sodium iodide symporter activity has returned to
5 normal.

6 I wonder if six weeks in our -- in the
7 subcommittee report could be amended to at least six
8 weeks in order to acknowledge the potential for a longer
9 period of time being necessary. I don't know how one
10 would assess how long a period of time between six weeks
11 and three months should be recommended, but certainly
12 for the provision of information to patients, in
13 accordance with the ALARA principles, so that
14 breastfeeding women would have time to allow at least
15 six weeks' cessation of breastfeeding before
16 administration of Iodine-131. Would you comment on
17 that?

18 MEMBER METTER: Yes. Actually, thanks for
19 bringing that up. There was a comment as far as the
20 minimal timeframe in regards to notifying the nursing
21 mother regarding her I-131 therapy issue with nursing,
22 and we did say it was going to be at six weeks. I have
23 no problem saying at least six weeks prior to the
24 radioiodine administration. Does anybody else on the
25 subcommittee have any comments?

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1 VICE CHAIRMAN ZANZONICO: This is Pat
2 Zanzonico. I have no problem either with that
3 language, meaning specifically 'at least six weeks.'

4 I think we all recognize that both medically and
5 logistically the longer that period of discontinuation
6 of breastfeeding begins prior to therapy, the more
7 problematic it becomes.

8 And so I think six weeks itself may be
9 somewhat problematic, but I have no problem at all with
10 that language, at least -- at least six weeks for
11 cessation prior to therapy.

12 MEMBER METTER: Thank you, Dr. Zanzonico.
13 Thank you as well for your comment on that. And any
14 other comments?

15 Okay. Dr. Alderson, I'll turn it back to
16 you.

17 CHAIRMAN ALDERSON: Well, thank you. I
18 believe that must conclude this report and discussion.
19 Are there other comments from people who are online?

20 OPERATOR: And if you have a question or
21 a comment from the phones, you may press star one at
22 this time. Make sure your phone is unmuted and record
23 your name. And to withdraw that request, you may press
24 star two. Once again, press star one for questions
25 or comments from the phones, and I'll stand by for

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1 questions or comments.

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

4 DR. MARCUS: Thank you. Pat, I think we're
5 in complete agreement on everything except the 500
6 millirem calculations. And I think it would be really
7 helpful to have both the 100 millirem and the 500
8 millirem, recognizing that for 21 years the limit has
9 been 500 millirem, and then the physician and the
10 lactating mother decide what ALARA provision is
11 appropriate.

12 Otherwise, what we have is something so
13 conservative that I think a lot of people won't want
14 to use it. I know that Mike and Hazel's paper
15 originally used 100 millirem, but Mike has changed his
16 mind and thinks 500 millirem calculations would be good.

17 And I think having both might be the best way to do
18 it. Then licensees can choose what seems most
19 appropriate, and we'll have at least the calculations
20 with which to make a good choice.

21 Thank you.

22 OPERATOR: Does that conclude the question
23 or comment?

24 DR. MARCUS: Yes, it does.

25 MEMBER METTER: May I say something on this

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1 regarding -- in our paper, the first part as far as
2 the current guidance, it does allude to a nursing mother
3 who has received, until byproduct material can be
4 released by a licensee, the total effective dose
5 equivalent to any other individual, including her
6 nursing child, is projected to not exceed five
7 millisieverts. But she must give guidance if it's
8 going to exceed one millisievert. So we have that in
9 our paper.

10 DR. MARCUS: Yes. But you don't have the
11 calculations.

12 VICE CHAIRMAN ZANZONICO: This is Pat
13 Zanzonico. I personally have no objections to
14 including a -- essentially a dual set of
15 recommendations. I mean, the heart of the report and
16 the key recommendations, of course, are the
17 recommendations for the duration of discontinuing
18 breastfeeding.

19 And we can certainly add an additional
20 column which gives those periods of time for a
21 100 millirem dose to the nursing infant and a 500
22 millirem dose to the nursing infant.

23 If I understand correctly, the NRC
24 obviously doesn't regulate breastfeeding, and we can
25 provide, as points of information, the recommended

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1 discontinuation periods for 100 and 500 millirem
2 limits, and the patient and their caregivers can then
3 choose as appropriate.

4 I have no objection, scientific or
5 otherwise, to that approach. I don't know if -- if
6 having dual recommendations in effect is problematic
7 from the NRC's point of view. But from a logistical,
8 scientific point of view, I have no objection to that
9 approach.

10 MS. HOLIDAY: Dr. Zanzonico and Dr. Metter,
11 NRC does not object to, if you want to amend the
12 subcommittee report to reflect these dual
13 recommendations, that's at your discretion.

14 MEMBER METTER: Thank you, Sophie. I
15 think if that's okay, we'll go ahead. Any other
16 comments from the subcommittee? Because I think we'll
17 go ahead and make those two recommendations as far as
18 listing on the table as Dr. Zanzonico had reflected.

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

21 MEMBER METTER: Yes.

22 MEMBER WEIL: I have no objection to
23 listing both sets of recommendations, but I would like
24 to know that they would be labeled with the agency that
25 recommends both the 100 and the 500 millisieverts

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1 threshold.

2 MEMBER METTER: Okay.

3 MEMBER WEIL: So that the chart or the graph
4 itself is labeled to indicate which agencies recommend
5 which threshold.

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

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

10 MEMBER METTER: Oh, I see. Okay. Thank
11 you.

12 Any other comments?

13 OPERATOR: And I am currently showing no
14 further questions or comments from the phones. Again,
15 as a reminder, if you have further questions or
16 comments, it is star one. Make sure your phone is
17 unmuted and record your name. And it is star two to
18 withdraw that request. And I'll stand by for any
19 further questions or comments at this time.

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

22 CHAIRMAN ALDERSON: All right. Thank you
23 very much.

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

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1 name.

2 CHAIRMAN ALDERSON: Certainly.

3 OPERATOR: One moment. Thank you.

4 Excuse me. Dr. Greenspan, your line is open for your
5 question or comment.

6 DR. GREENSPAN: Thank you very much. I
7 just had a quick comment as a follow up to
8 Dr. Zanzonico's request for references for gamma ray
9 constants. I'm traveling this week, but I will be glad
10 to provide them next week. I hope that won't be too
11 late. Thank you.

12 VICE CHAIRMAN ZANZONICO: This is Pat
13 Zanzonico. Yes, Dr. Greenspan, that would be certainly
14 soon enough. The additional analyses I'm committing
15 to are going to take a bit of time, and they certainly
16 won't be concluded by next week, so next week will be
17 soon enough.

18 DR. GREENSPAN: Thank you very much.

19 OPERATOR: Thank you. And I'm currently
20 showing no further questions or comments at this time.

21 CHAIRMAN ALDERSON: Good. Thank you.
22 That means that we will now proceed with the next part
23 of this public conference call. That will be the report
24 from Dr. John Suh's subcommittee on the physical
25 presence requirements for the Gamma Knife Icon. I will

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1 turn the conversation over to Dr. Suh.

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

6 CHAIRMAN ALDERSON: Yes, certainly.

7 That's fine. Let's do that.

8 MEMBER METTER: Can I make a motion to
9 endorse the amended reports?

10 PARTICIPANT: Second.

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

14 MEMBER METTER: Okay. Dr. Zanzonico?

15 VICE CHAIRMAN ZANZONICO: Yes. The
16 amendments will include acknowledgment of the benefits
17 of breastfeeding. They will include correction as
18 needed of the specific gamma ray constant values. They
19 will include conversion of the system of units from
20 conventional to SI. There will be an expanded
21 dosimetric analysis of radioiodines as a function of
22 the age and thyroid mass of the child, and also include
23 other medical radionuclides -- radioisotopes of iodine.

24 We will include at least two additional
25 references as cited by Drs. Marcus and Sabin. And we

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1 will include recommendations or recommended cessation
2 periods of time based on both a 100 and a 500 millirem
3 effective dose to the nursing child.

4 MS. HOLIDAY: Okay. Thank you, Dr.
5 Zanzonico.

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

9 MS. HOLIDAY: Thank you. Okay. Dr.
10 Alderson, now that there is a motion, can you call for
11 the vote?

12 CHAIRMAN ALDERSON: All right. All in
13 favor?

14 (Chorus of ayes.)

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

17 CHAIRMAN ALDERSON: All right. So as I
18 stated a moment ago, I'll repeat now, it is now time
19 for us to consider the report on the physical presence
20 requirements for the Gamma Knife Icon, that
21 subcommittee report. That subcommittee is led by
22 Dr. John Suh. Dr. Suh, you're on.

23 MEMBER SUH: Okay. Thank you, Dr. Alderson.
24 I want to first thank the subcommittee members, Dr.
25 Ron Ennis and Laura Weil, and also thank Sophie Holiday

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1 for her staff resource support.

2 So I will -- the charge to the subcommittee
3 was to propose the appropriate physical presence
4 requirements for Leksell Gamma Knife® Icon™
5 radiosurgery units. And I just want to go through just
6 a little bit about the gamma knife. The gamma knife
7 is a very well-established treatment for patients with
8 various benign and malignant brain tumors, vascular
9 malformations, and functional disorders, including
10 trigeminal neuralgia.

11 The first gamma knife in the United States
12 was installed at the University of Pittsburgh in 1987,
13 and over the years the gamma knife has evolved and in
14 2006 the Perfexion™ unit was introduced, which allowed
15 for the authorized users to be inside the treatment
16 unit.

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

24 In terms of the current physical presence
25 requirements in 10 CFR part 35, it requires an

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1 authorized user with appropriate training and
2 experience in radiation oncology and an authorized
3 medical physicist to be physically present throughout
4 all treatments involving the unit. And physical
5 presence has undergone some evolution. Initially, it
6 was defined as within hearing distance of normal voice,
7 and as part of a regulatory issue summary it was further
8 defined to be speaking in a normal conversational tone,
9 not a raised voice. And they made a comment that a
10 distance of 20 feet may not be close enough to adequately
11 hear and respond to an emergent situation.

12 The rationale for changing the physical
13 presence requirements is that the gamma knife unit,
14 as I mentioned, has evolved through the years. It is
15 important that any change we make allow the authorized
16 user to address an emergent situation and also to verify
17 that a correct dose was delivered.

18 If you look at the past 10 years of the NMED
19 report, there have been 10 reportable events involving
20 the Perfexion™, and only a minority of these events
21 occurred during a treatment.

22 So from the Perfexion™ in -- there has been
23 an evolution to a newer unit called the Icon™ system.

24 Some of the fundamental differences with the Icon™
25 system is that it does allow for the option of a

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1 thermoplastic frameless mask rather than a frame. The
2 majority of centers using the Icon™ system still use
3 a frame-based system rather than a mask-based system.

4 It does give the option for those patients who may
5 benefit from some type of fractionated approach.

6 Number two is it allows the ability to perform
7 integrated stereotactic cone beam CT, which provides
8 stereotactic reference for patient setups.

9 And number three is it also has a high
10 definition motion management for mask-based
11 treatments, which allows us to confirm that the
12 treatment is being delivered to the target itself.

13 There was a proposal from Elekta on
14 April 26th about the Gamma Knife® Icon™, and their
15 proposal is that an authorized user and authorized
16 medical physicist be physically present during the
17 initiation of all treatment involving a unit.

18 Number two is to have an authorized medical
19 physicist present throughout all patient treatments.

20 And number three is that an authorized user
21 physically be present in the department during patient
22 treatment and immediately be able to come to the
23 treatment room in case of emergency.

24 Based on the -- looking at the current
25 physical presence requirements, the evolution of the

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1 Icon unit, the recommendations from the subcommittee
2 is that the authorized user and authorized medical
3 physicist be physically present during the initiation
4 of all treatments involving the Icon™, and that the
5 authorized medical physicist be physically present
6 throughout all treatments of the unit itself.

7 We have made a recommendation that the
8 current physical presence requirements for the
9 authorized user be modified to allow the authorized
10 user to be close enough to the console area to respond
11 quickly to any issues that may arise.

12 The definition we came up with is that within
13 a two-minute walk of the Icon console area and
14 immediately available to come to the treatment room.

15 So it is very important that with this definition of
16 physical presence, the authorized user cannot be
17 involved in another procedure that would prevent him
18 or her to come immediately to the gamma knife in case
19 of an emergency.

20 In addition, we felt that it was important
21 that we do not use the definition of a department as
22 "department" can have different meanings to different
23 centers. So one could be stated that it's part of a
24 department, but the department could be physically a
25 long walk away. So we felt that there should be some

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1 time restraint in terms of what constitutes being
2 physical presence in terms of this newer definition.

3 If there is an interruption of treatment
4 secondary to a medical or mechanical event, the
5 authorized user must return to the Gamma Knife® Icon™
6 console area to evaluate patient and to review any of
7 the medical -- mechanical issues along with the medical
8 physicist.

9 And at the conclusion of treatment, the
10 authorized user must be present at the Icon console
11 to discuss any treatment or patient issues with the
12 patient, physicist, and a nurse.

13 The subcommittee felt that with these
14 modifications, in terms of current physical presence
15 requirements, it would allow more flexibility to the
16 authorized user.

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

23 Any change that occurs to the current
24 physical presence requirements should take into account
25 that the culture of safety quality be supported, given

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1 the superb track record for quality and safety with
2 the gamma knife.

3 Thank you. That concludes my report, Dr.
4 Alderson.

5 CHAIRMAN ALDERSON: All right. Thank you.
6 Are there comments?

7 MEMBER SHEETZ: John, this is Mike Sheetz.
8 I have some comments.

9 CHAIRMAN ALDERSON: Please.
10 MEMBER SHEETZ: I think the subcommittee
11 provided an excellent report and overview of the
12 technological advances in gamma knife treatment since
13 the process has become more efficient allowing for more
14 treatments, and multiple targets can be treated in a
15 single session.

16 And they pointed out, based on the small
17 number of medical events involving modern gamma knife
18 models, it is, therefore, appropriate to evaluate the
19 required physical presence requirements for gamma knife
20 to see if they should be revised.

21 Based on our experience here at the
22 University of Pittsburgh where we have had every model
23 like the gamma knife, and we were the first to license
24 the U model in 1987, I have some comments with respect
25 to the recommendations of the subcommittee, if I may

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1 proceed with those.

2 CHAIRMAN ALDERSON: Please.

3 MEMBER SHEETZ: I agree with the
4 recommendation number one that the AU and AMP need to
5 be physically present at the initiation of all
6 treatments.

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

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

24 So I'll throw that up for consideration.
25 Again, it would be consistent with the HDR requirements,

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1 and it would eliminate any ambiguity in response times,
2 and it would assure that appropriate personnel are
3 present to respond to any patient medical issues.

4 I agree with recommendation three that the
5 AU must return to the gamma knife console for the
6 interruption of treatment secondary to medical or
7 mechanical issues.

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

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

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1 treatments.

2 In our experience, less than 10 percent of
3 the gamma knife patient cases qualify for mask-based
4 treatments. There have been an extremely low number
5 of medical events with Perfexion™ that have been pointed
6 out involving thousands of patient treatments
7 demonstrating a highly reliable treatment technology.

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

14 And that concludes my comments.

15 CHAIRMAN ALDERSON: Thank you. Dr. Suh?

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

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1 that is too -- that is too ambiguous. So we felt that
2 was not a good starting point.

3 And we grappled at the time -- we needed some
4 type of time standpoint. And I do agree with you that
5 there could be some ambiguity in terms of regulatory
6 compliance. I actually have looked at your comments.

7 I actually thought about it.

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

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

24 In terms of point -- so in terms of authorized
25 user returning, I'm glad that you agree with that

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1 comment. I do think it's important for the authorized
2 user to return.

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

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

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

24 In terms of number five, in terms of whether
25 or not the Icon™ and the Perfexion™ are similar units,

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1 although the fundamental makings of the Icon™ are very
2 similar to the Perfexion™ unit, there is the opportunity
3 to use a cone beam CT device for the frame-based
4 treatments.

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

13 So I don't feel that the Perfexion™ and the
14 Icon™ are similar. So I am not in support of modifying
15 physical presence requirements for both Perfexion™ and
16 Icon™. I would propose that we change the physical
17 presence requirements for just the Icon™ unit 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 little
22 bit of ambiguity with that, although I don't think it
23 will be a lot because it does specify a time which you
24 can measure and walk. And of course people can walk
25 slightly faster or slower, but I don't think it's

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1 tremendously ambiguous.

2 So I'm comfortable with that. The notion
3 of instead requiring another physician to be there under
4 the supervision, I would be comfortable with that, too.

5 That is more restrictive on our users, I think, than
6 the proposed definition that our subcommittee came up
7 with.

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

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

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

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

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

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

21 And on the final point of Perfexion™ versus
22 Icon™, frankly, I would defer to Dr. Suh's judgment.

23 He has a lot more experience with these units than
24 I. So I don't have any particular opinion beyond his
25 on that.

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1 I think I covered all the points. But if
2 there is something else, Mr. Sheetz, please remind me.

3 MEMBER SHEETZ: This is Mike Sheetz. Thank
4 you for your consideration and responding to those --
5 all of my comments.

6 So I guess, for clarity, you are recommending
7 these revisions for the Icon™ unit for both frame-based
8 and mask-based treatments. Is that correct?

9 MEMBER ENNIS: That is correct. Yes.

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

16 So, again, I guess I still go back to
17 frame-based treatments on Icon™ and Perfexion™ are
18 identical in practice.

19 MR. OUHIB: Hi. This is Zoubir.

20 CHAIRMAN ALDERSON: Go ahead.

21 MR. OUHIB: On item number two, you know,
22 trying to use the HDR regulation type of thing, I think
23 it's a good idea. However, there are institutions that
24 might not be as fortunate to have the luxury of a
25 physician under the direct supervision of an authorized

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1 user.

2 So perhaps consideration would be to use one
3 or the other; in other words, to keep the two-minute
4 option and perhaps -- or the presence of a physician
5 under the direct supervision of an authorized user.

6 CHAIRMAN ALDERSON: Are there further
7 comments? Is there anyone that would like to comment
8 on that statement?

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

19 You know, in terms of this proposal of either
20 an authorized user or physician under the supervision
21 of authorized user be present, it does -- it's probably
22 a clearer definition, although it is somewhat more
23 restrictive. And for a smaller center that may not
24 have the luxury of having another physician involved,
25 I can see this being a more restrictive definition for

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1 gamma knife.

2 Not all gamma knife centers have multiple
3 physicians who are: a) trained, and b) have an interest
4 in being involved in gamma knife.

5 In terms of doing both, I guess I have mixed
6 feelings about whether or not both is a good option.

7 I think we should stick with one option if we are going
8 to go ahead with changing the current physical presence
9 requirements, which was the charge of the subcommittee
10 to begin with.

11 CHAIRMAN ALDERSON: Further comments? I
12 think we still need to work to clarify this a bit.
13 I'm going to take the prerogative here to indicate what
14 I think is being said, and then I'd like to get, John,
15 your comments and that of the Committee to clarify this.

16 So I am hearing that regarding the comment
17 of extending this new approach to both the Icon™ and
18 the Perfexion™, I believe that the Committee is saying
19 that it would choose to stay with the Icon™ alone, that
20 there should be -- the physician should be present at
21 the end of the treatment, so that they can talk to the
22 patient.

23 Am I correct on the Committee's position on
24 those two issues?

25 MEMBER SUH: This is John Suh speaking again.

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1 Yes, I do believe that the Icon™ and Perfexion™ are
2 different units.

3 CHAIRMAN ALDERSON: Yes.

4 MEMBER SUH: And your second point about
5 being present at the conclusion of treatment, like Ron,
6 I feel very strongly that it is important to close the
7 loop when treating patients with high dose/high
8 precision radiation that is offered with the Icon™ Gamma
9 Knife® unit.

10 CHAIRMAN ALDERSON: Right. Am I correct
11 that Dr. Ennis and Laura Weil agree with those
12 positions?

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

20 But I do feel like there could be more subtle
21 or minor safety concerns, issues that might have
22 happened that would not stop the treatment and would
23 not be a misadministration, but might be helpful for
24 the team to know going forward for the next case or
25 the next patient, where things weren't perfect, that

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1 it's really important to have that kind of -- well,
2 they call it a huddle nowadays, right? Doing
3 essentially a mandated huddle from a safety point of
4 view at the end of treatment, which will only really
5 happen efficiently and effectively, in my opinion, if
6 we mandate that everyone gets together at the end.

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

9 MEMBER WEIL: No.

10 MEMBER SUH: No.

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

17 I'm going to turn this back to Dr. Suh to
18 try to see if we can navigate our way through that
19 particular concern, which seems to be the significant
20 one remaining in this discussion.

21 MEMBER SUH: So I have been thinking about
22 this since, you know, Michael sent this to me. As I
23 said, I am -- I like his suggestion, but I do agree
24 that it is more restrictive. And, again, it should
25 be very apparent. You know, a two-minute walk I don't

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1 think should be that ambiguous in terms of responding
2 to an emergency or if there is an issue with a patient.

3 But my personal feeling, my recommendation,
4 is that the subcommittee report of the altered current
5 physical presence to allow for the authorized user to
6 be within a two-minute walk of the gamma knife console
7 area is appropriate and will allow the authorized user
8 to respond to any immediate medical needs.

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

11 MEMBER ENNIS: I do.

12 CHAIRMAN ALDERSON: Laura?

13 MEMBER WEIL: Yes, I do.

14 CHAIRMAN ALDERSON: Okay. So that's also
15 clear from the standpoint of the subcommittee. Are
16 there other comments before we open this up to people
17 who might be on the phone lines?

18 So with the help of the operator, we will
19 now take comments on any of these issues from people
20 who are on the phone?

21 OPERATOR: Thank you. And, again, as a
22 reminder, if you have a question or a comment from the
23 phone, please press star one at this time. Make sure
24 your phone is unmuted and record your name to introduce
25 your question. And to withdraw that request, you may

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1 press star two. Once again, for questions or comments,
2 press star one and record your name at this time.

3 And one moment. We'll stand by for questions
4 or comments. One moment, please. And we do have a
5 question or comment from Susan Lohman. Your line is
6 open.

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

12 And at this time, I would like to urge the
13 subcommittee and Committee to move forward with the
14 subcommittee's recommendation as it was proposed and
15 possibly in the future come back to look at the inclusion
16 or continued exclusion of Perfexion™.

17 And myself, as a representative of Elekta,
18 would be more than willing to provide any subject
19 material necessary to proceed as such.

20 Thank you.

21 CHAIRMAN ALDERSON: Do we have other
22 comments?

23 OPERATOR: Yes, we do have another question
24 or comment. And our next question or comment is from
25 Frank Tran. Your line is open.

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1 MR. TRAN: Yes. This is Frank Tran in
2 Region III, NRC. I have a comment on the rule with
3 the HDR of exactly they -- they didn't require direct
4 supervision from an authorized user or a trained person.

5 It just says under supervision. So I believe the key
6 is not that. So I just want to comment on that.

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

11 MR. TRAN: Okay. So earlier I believe that
12 Mike mentioned about the rule under -- that required
13 authorizer user to be -- or a trained person to be
14 present over the -- under the rule for the HDR. Another
15 person mentioned that there should be direct
16 supervision.

17 However, under the rule for the HDR, it is
18 not a direct supervision, just a supervision, either
19 direct or not direct. So there's the comment for that.

20 CHAIRMAN ALDERSON: All right. Did people
21 understand the comment?

22 PARTICIPANT: Yes.

23 CHAIRMAN ALDERSON: Okay. Are there
24 further comments?

25 OPERATOR: I am currently showing no further

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1 questions or comments at this time. And, again, as
2 a reminder, that is star one. Make sure your phone
3 is unmuted and record your name. And it is star two
4 to withdraw that request.

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

8 CHAIRMAN ALDERSON: So, Dr. Suh, I'm going
9 to summarize here how I think this conversation has
10 evolved. I think we are -- we have accepted the --
11 we have listened to all of the comments. We have made
12 comments in return. I believe that we're at the point
13 where we are ready to accept the proposal as it was
14 originally recommended. Is that how you also
15 understand the comments?

16 MEMBER SUH: Yes, Dr. Alderson.

17 CHAIRMAN ALDERSON: Okay. Well, in that
18 case, are we in fact ready to -- is the subcommittee
19 and the -- are the ACMUI recommended as -- to accept
20 the report as it was originally proposed? All those
21 in favor?

22 (Chorus of ayes.)

23 CHAIRMAN ALDERSON: Any opposed? Thank
24 you. This report is accepted in its original proposed
25 form.

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1 MS. HOLIDAY: Dr. Alderson, if I may, I'm
2 sorry, I didn't catch who made the motion and who
3 seconded the motion.

4 CHAIRMAN ALDERSON: I believe it was implied
5 that Dr. Suh was making the recommendation, I believe.

6 MEMBER SUH: Yes. On behalf of the
7 subcommittee, I propose that we accept the current --
8 sorry, the physical presence requirements of the
9 Leksell Gamma Knife® Icon™ that as submitted on behalf
10 of the subcommittee members.

11 VICE CHAIRMAN ZANZONICO: Sophie, this is
12 Pat. I'll second it.

13 MS. HOLIDAY: Thank you.

14 CHAIRMAN ALDERSON: Good.

15 MS. HOLIDAY: And then, if I understand, was
16 this a unanimous endorsement, or were there any
17 dissents or abstentions?

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

20 MS. HOLIDAY: Okay. Thank you.

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

23 MS. HOLIDAY: No. I would just like to thank
24 the subcommittee members for putting forth all of the
25 effort for both Dr. Metter's subcommittee and Dr. Suh's

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1 subcommittee, for their thorough reviews and their
2 reports. I would also like to remind the ACMUI members
3 and other participants on the phone that ACMUI will
4 be holding another public teleconference in two weeks
5 on March 1st from 2:00 p.m. to 4:00 p.m. eastern.

6 The topic of that teleconference will be the
7 subcommittee report for the training and experience
8 requirements under all modalities in 10 CFR part 35
9 with a focus on 35.300 uses.

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

12 Thank you.

13 CHAIRMAN ALDERSON: Well, thank for everyone
14 who was on the call today.

15 Mr. Bollock, anything you would like to say
16 in the end?

17 MR. BOLLOCK: No, thank you, Dr. Alderson.
18 Appreciate everyone's time.

19 CHAIRMAN ALDERSON: I believe, Sophie, that
20 we have concluded our business. Thank you all,
21 everyone.

22 (Whereupon, the discussion of the draft
23 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 "luteum", 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,

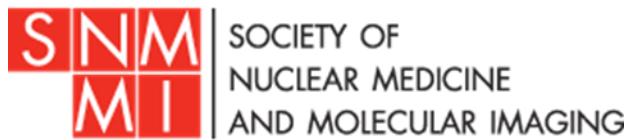


Carol S. Marcus, Ph.D., M.D.

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Michael G. Stabin
Chair, RADAR 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.

- 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"

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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,

Bennett S. Greenspan, MD, M.S.

Bennett S. Greenspan, MD, FACNM, FACR
President, SNMMI

U.S. Nuclear Regulatory Commission (NRC)

February 12, 2018

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