Official Transcript of Proceedings

NUCLEAR REGULATORY COMMISSION

Title: Advisory Committee on the Medical Uses of Isotopes

Docket Number: (not applicable)

Location: (telephone conference)

Date: Tuesday, March 8, 2005

Work Order No.: NRC-266 Pages 1-77

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NUCLEAR REGULATORY COMMISSION

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ADVISORY COMMITTEE ON MEDICAL USES OF ISOTOPES

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Tuesday, March 8, 2005

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Telephone Conference Call

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The above-entitled matter came on for hearing, pursuant to notice, at 1:30 p.m., Leon S. Malmud, M.D., Chair, presiding.

COMMITTEE MEMBERS PRESENT:

LEON S. MALMUD, M.D., Chair

JEFFREY F. WILLIAMSON, Ph.D., Member, Subcommittee Chair

EDGAR BAILEY, Ph.D., Member

DAVID DIAMOND, M.D., Member

DOUGLAS F. EGGLI, M.D., Member

RALPH P. LIETO, Member

SUBIR NAG, M.D., Member

THOMAS SCHENTER, M.D., Member

SALLY SCHWARZ, R.Ph., Member

ORHAN SULEIMAN, Ph.D., Member

RICHARD J. VETTER, Ph.D., Member

NRC STAFF PRESENT:

THOMAS H. ESSIG, Designated Federal Official

IVELISSE CABRERA

CINDY FLANNERY

DONNA BETH HOWE

DORIS LEWIS

ANGELA McINTOSH

RONALD ZELAC, Ph.D.

ALSO PRESENT:

DR. LOUIS POTTER

DR. ROBERT SCHENIR

P R O C E E D I N G S

(1:30 p.m.)

MR. ESSIG: My name is Tom Essig. I am the Designated Federal Official for this meeting. I am pleased to welcome you to this publicly noticed meeting conference call of the ACMUI. I am Acting Deputy Director of the Division of Industrial Medical Safety in the Office of Nuclear Material Safety and Safeguards at the NRC. I have been designated as Acting Federal Official for this Advisory Committee in accordance with 10 CFR Part 7.11.

This is an announced meeting of the committee. It's being held in accordance with the rules and regulations of the Federal Advisory Committee Act, and the Nuclear Regulatory Commission. The meeting was announced in the February 22nd, 2005 edition of the *Federal Register*.

The function of the committee is to advise the staff on issues and questions that arise on the medical use of byproduct material. The committee provides counsel to the staff, but does not determine or direct the actual decisions of the staff or the commission. The NRC solicits the views of the

committee and values them very much.

I request that whenever possible we try to reach a consensus on various issues that we will discuss during this conference call, but I also value minority or dissenting opinions. If you have such, please allow them to be read into the record.

As part of the preparation for this meeting, I have reviewed the agenda for the members and employment interest, and based on the general nature of the discussion that we're going to have today, I have not identified any items that would pose a conflict of interest for members. If during the course of our business members determine that they have such a conflict on matters before the committee, please state it for the record, and recuse yourself from that particular aspect of the discussion.

At this point, I would like to perform a roll call of members that may be participating today. I recognize that a preliminary roll call had already been accomplished, but let's do it this time for the record.

(Roll Call.)

MR. ESSIG: Okay. First, I'll go to the NRC Staff who are present with me here in the room, or

any others that may be on the line to identify themselves.

MS. CABRERA: Ivelisse Cabrera.

MS. HOWE: Donna Beth Howe.

MS. LEWIS: Doris Lewis.

MS. FLANNERY: Cindy Flannery.

MS. McINTOSH: Angela McIntosh. That's spelled A-N-G-E-L-A M-C-I-N-T-O-S-H. If you want your name spelled correctly, you probably have to spell your name for the record.

DR. ZELAC: Last but not least, Dr. Ronald Zelac, Z-E-L-A-C.

MR. ESSIG: Okay. Are there any other members of the NRC Staff who may have called into the bridge? Okay. Hearing none, I believe we have a guest with us, Dr. Louis Potter. Is that correct?

DR. POTTER: Yes.

MR. ESSIG: Okay. And, Dr. Potter, I would offer that depending on the status of our discussion today, where we leave things, if it seems prudent that we, and if you're available and are interested, and would like to attend our Full Committee Meeting on the 20th and 21st of April, we would be willing to pay for invitational travel for you to come to that

meeting, if it turns out that it seems in our mutual best interest, and you're available.

DR. POTTER: Yes. No, that would not be a problem.

MR. ESSIG: Okay. And let me mention then that following the discussion of each agenda item, the Chair, Dr. Malmud, at his option may entertain comments or questions from members of the public who are participating with us today. At this point, Dr. Malmud, I turn the meeting over to you.

DR. MALMUD: Thank you, Tom. I think the purpose of the meeting is to discuss the issue of the 20 percent variation or variability in the dosimetry from bracheotherapy of the prostate gland, and related to it, the question of what happens when the seeds are implanted in other tissue or organs besides the prostate.

A sub-subject was the concern that the calculation of the dose was done after the time of the therapy, and there needed to be knowledge on the part of those who are not radiation oncologists regarding the rationale for doing the dosimetry after the administration rather than prior to or during the administration.

I think that summarizes my understanding of the purpose of this. Are we in agreement as to the purpose?

DR. WILLIAMSON: Jeff Williamson. I think that the way the definitions of written directive to the current medical event rule is written, the defining characteristic is not prostate bracheotherapy, but any permanent seed implant.

DR. MALMUD: Thank you.

MR. ESSIG: Dr. Malmud, this is Tom Essig. One other administrative matter that I should have mentioned earlier; and that is, we should have any members of the public who are participating with us today to identify themselves so the court reporter will, in the event that they choose to, you wish to recognize them toward the end of the call, and they wish to offer some views, that the court reporter will have the proper spelling of their names. So if we could go ask any members of the public to identify themselves or organizational members; would you please do so now.

MS. FAIROBENT: Lynn Fairobent, AAPM.

MS. DRUMMOND: Roshunda, R-O-S-H-U-N-D-A, Drummond, D-R-U-M-M-O-N-D, and I'm with Astro, A-S-T-R-O.

MS. MARTIN: Melissa Martin, M-E-L-I-S-S-A M-A-R-T-I-N, and I am on the ACR Government Relations Committee.

MR. ESSIG: Thank you.

MR. CANNON: Hugh Cannon with the Society of Nuclear Medicine.

MR. ESSIG: Thank you.

DR. MALMUD: Do we have two representatives from the ACR, both Timmy Moran and Melissa Martin?

MR. MORAN: Yes. Also on the call is Ariel Gonzalez, A-R-I-E-L, last name G-O-N-Z-A-L-E-Z. I am with the ACR Government Relations Staff.

DR. MALMUD: Thank you. Any other members of the public? If not, let's move ahead. Thank you.

All right. The purpose of the meeting is to discuss the issue with regard to the 20 percent variability in permanent seed implantation. We were focusing on the prostate, but as Dr. Williamson points out, the issue really is permanent seed implantation.

During the meeting of the committee, there was an obvious lack of knowledge among some of us, myself, radiation oncologists regarding the methodology for administering bracheotherapy, and also

for the rationale in calculating the dosimetry. A memo to us from the ACR, which is dated February 25th, very concisely summarizes the issue. I hope that you all have a copy of that memo dated February 25th. It was from the ACR. As we were reminded at the beginning of the meeting, it is solely from the ACR, not from other organizations. It's signed by James Borgsted, the Chair of the American Radiology. Do you all have copies of that? Thank you.

Dr. Potter has been asked and has agreed to serve as a consultant, because in our inquiries nationally, he is felt to be one of the most experienced prostate bracheotherapists in the United States, respected widely. And for that reason, if I may, since his time with us is limited, if we may ask him to make a few statements regarding permanent seed implantation and bracheotherapy. Dr. Potter.

DR. POTTER: All right, thanks. I didn't realize that the call would be as formal as it is, and I do appreciate the opportunity to make a couple of comments, just in terms of my background. I'm a private practicing physician on Long Island. I started doing bracheotherapy in 1991. I was at North Shore University Hospital, if anybody knows, on Long Island,

and then was in private practice for another two years. And then in 1997, joined the faculty of Memorial Sloan-Kettering, where I stayed until about a year ago, and now I'm back in private practice.

I formed and developed what I call the New York Prostate Institute, which is basically my clinic. I've done about 2,400 implants. I have about 38-39 peer review publications on seeds. I co-authored about four or five book chapters, and I sat on the committee of the ACR that formed the guideline that the quote from Dr. Borgsted's letter is on. I've also worked on a committee that was put together by the American Bracheotherapy Society last year in terms of looking at normal tissue toxicity following prostate bracheotherapy.

So having said that, I think that it's important, and I applaud the committee or the NRC, the Commission, in terms of trying to come up with some sort of uniform definition of mis-administration. I think there's enough confusion between multiple State Departments of Health as to exactly what the definition of mis-administration is, and how it should be interpreted on the local level; that having a national policy probably would be helpful.

Just as a background in terms of how things have changed and evolved with prostate bracheotherapy, when I started in 1991, early 1992, there was no real ability for doing any sort of analysis of the implant, so that the total activity of the isotope that was used for performing the procedure was calculated based on the prostate volume, and using nomograms that converted that volume to total activity that was created by Lowell Anderson, and modified by Mt. Sinai and a couple of others, was really the determining factor. So I know from the New York State experience that the Department of Health was really concerned specifically with the total activity that was delivered, and that was based on those nomograms. And they would look at the physicist's involvement in terms of making sure that the analysis of the nomogram was done correctly, and that the appropriate total activity was delivered. And clearly, obviously, you take the total activity and you divide it by the activity per seed, which gives you the number of seeds, so that I don't want to confuse the issue at all with the number of seeds being important, because you can order high activity or low activity seeds, completely independent. It's all based on the total activity and the prescribed dose.

Over the ensuing years, and the physicists can go into it in more detail, there were some changes in the definition of how the activity was defined for each of the Iodine and the Palladium. And I guess around 1994 or so, some of the CAT scan-based dosimetry systems starting coming online and were used for analyzing better the dosimetry of prostate bracheotherapy. And although some of those initial dosimetry systems were for external beam, they were sort of co-opted for bracheotherapy. They were not necessarily specific for bracheotherapy, but they gave us the first hint that perhaps there is something to dosimetry for at least analyzing the implant after its performed in terms of trying to define some sort of quality measurement to the implant. And that was designed more or less for understanding the results, the biochemical results of the treatment, not necessarily for defining mis-administration.

The information from the concept of post implant dosimetry has evolved, and the question is now really can we use some of that information to define mis-administration. One of the things that we've learned, and I think it's pointed out in Dr. Borgsted's note, that there are some issues with the timing, and

what would represent an optimal timing for performing a CT Scan of the implant after bracheotherapy in terms of establishing an appropriate dosimetry. And although the ACR guideline recommends two to four weeks, there are plenty of centers that are doing it day one, or the day of the procedure for logistical reasons in that it's sometimes difficult to get the patients to come back. And the limitations of that, and the variabilities of that, are that you can have some acute edema, swelling of the prostate, which affects its volume and its size, and so that clearly impacts on your dosimetry analysis.

I think what's been published in the literature, I know that I've published on it, that for centers doing dosimetry, that there be some degree of consistency in how they do it. And so, if it's a referral center or in a rural location where coming back two to four weeks is difficult, that they develop a policy internally that's consistent so that the dosimetry across the board for that particular clinic represents the bias of the timing associated with performing the dosimetry, versus the opportunity to do it somewhere between two and four weeks, which is sought to be after a lot of the acute edema has resolved so that

you're back to more or less a normal prostate volume.

But the problem that I see in terms of defining mis-administration by the dosimetry, we could get into a detailed discussion as to what parameters are established, whether it's v-100 or the d-90, or d-100, is that those values are absolutely subjective based on the physician or the physician's assistant, or whoever may be involved in contouring the prostate so that you can artificially sort of create dose distribution curves that are absolutely perfect regardless of what you're doing. And so that to define a mis-administration definition on something that is as subjective as prostate contouring on a CT Scan, I think is going to be problematic. I think it will encourage physicians or group practices to really contour to meet the definition, rather than to contour to really understand the issue of the quality of the implant.

Changing the subject a little bit, I was involved in a panel that looked at normal tissue dose, and the toxicities associated with the rectum, the bladder, and other soft tissue within the pelvis, and the fact is that there really is no consistency in the literature as to what defines an overdose or an underdose, say to the rectum or the bladder, that would

then sort of cross some sort of threshold that would be associated with intolerable degree of toxicity. And, in fact, a pretty good exhaustive review of the literature indicates that we aren't even in agreement as to what definition should be used for the normal tissues in terms of a d-5, or a d-90, the urethra, or the rectum, and the biases associated with contouring of the rectum, do you contour the rectal volume that's just below the prostate, or do you extend it a centimeter cephalad codad. Because if you're calculating a dose to a volume, obviously the dose - and you want to lower the dose if you contour more rectum away from the prostate, and you're going to inflate the volume relative to the potential dose, so basically the best that the American Bracheotherapy Society can come up with, and our paper is going to be published I think next month or in two months in bracheotherapy, is to come up with a recommendation as to how the rectum should be contoured, how the bladder should be assessed, how the urethra should be assessed, and how the penile bulb should be assessed for future study in terms of complications.

So having said that, I've also been aware of - I used to do a fair amount of malpractice

consulting, and I am aware of a lot of cases where seeds wind up in recto prostatic tissues, and ulceration develops. I'm also aware of some cases where patients would undergo salvage prostatectomy after bracheotherapy, and only two seeds are in the prostate and 60 something seeds are somewhere else, who knows where. And so that there are issues in terms of patient safety that I think are important. It's just a matter of eliminating some of the subjectivity from what we would consider the standard dosimetric definitions, the d-90, the v-100s, which are truly subjective.

The other thing, just to finish out and round out my comments real quick, is that I am currently performing interoperative realtime dosimetry. Now personally, I think that that sort of represents the future a little bit where we are doing real dynamic seed assessment in the operating room, where literally we're following the seeds as they're being dropped by the mick gun. And in our first publication on the technique, we showed a direct correlation to the post implant dosimetry, and I'm going to be updating that data this spring, and submitting it for abstract for next year. But there appears to be an opportunity for really assessing in the operating room, that potentially

negates even the need for post implant dosimetry as we currently do it now, which is the CAT Scan two to four weeks or so. And there was an article, it was a French study that was done, that specifically made that recommendation. If you can walk out of the OR and have a pretty good idea of what's going on, then why do you have to bring the patient back later for it? So I think there are some changes in terms of how we're doing the cases. I know that the ACR guideline does say two to four weeks, but I also know that that guideline is constantly being updated to reflect current practices.

So I don't know if that's helpful or not for the committee, but that's my sort of opening two cents.

DR. MALMUD: Thank you, Dr. Potter. Are there questions for Dr. Potter?

DR. SCHENIR: This is Bob Schenir. I just have two quick questions. I may have missed it, but have you done both Palladium 103 and Iodine 125?

DR. POTTER: Yes. I would say that I have done probably close to about 70 percent Palladium, 30 percent Iodine in the 2,400 or so patients.

DR. SCHENIR: My second question is, I'm a nuclear physicist by background. I've done thousands of MCNP calculations, and I'm not sure what's going on

there, but certainly we can accurately calculate the dose using a monocarlo code like MCNP for these type of situations. Does that play a role, or how would you expect that to play a role?

DR. POTTER: I'm not specifically sure what you're suggesting.

DR. NAG: Hi. This is Dr. Nag. Maybe I can step in. Basically, Mr. Schenir, the problem is not calculating the dose back to the seed. I mean, that's not the problem. The problem is trying to quantify what amount of that dose is within the volume of the prostate. That would seem very simple, except that you don't really know exactly where the prostate is. And as Dr. Potter was saying, it may be very subjective as to how you draw the volume of the prostate on CAT Scan. On an MRI, you are able to define the prostate a little better than you can on the CAT Scan, but the practical way to determine the volume is by doing it on a CAT Scan. And there you see a block, and someone may see a bigger volume in the prostate, while others may see a smaller volume in the prostate.

DR. SCHENIR: Thank you.

DR. POTTER: Yes. No, the issue is - and I'll tell you, it's not absolutely well-defined as to

what the standard is - but we QA all the seeds. We throw them in a well and we're calculating the seeds. In my practice we do 100 percent of the seeds. We do them in group batches, and we've done some analysis as to how it should be, so it's not a matter of the shipping label versus what it really turns out.

I know that early, early on, I think in the mid-1990s, there were a couple of cases where the seed activity - I think for Iodine, I know there were a couple of cases where the seed activity was off by a factor of 10, and there was issues related to that. But I think that most centers now are performing some degree of quality assurance from the delivery end of the seeds. And that, in and of itself, as a result really has very little clinical significance. But to the degree that centers should be checking, whether they check 10 percent or the square root of the total number of seeds, or however one would want to define that, if the committee felt that there was a need to define that the seeds were checked and that's part of the hot lab records, then that does represent a safety issue that would be significant. It's just that I don't see that as a hot button issue.

DR. WILLIAMSON: Dr. Potter, this is Jeff

Williamson. I think that reviewing the past documents from some of our recent teleconferences, I think there was a fair amount of agreement that using dose to express a error criteria, or medical event criteria, was fraught with difficulties, for exactly the reasons you said; that it was subjective.

My question to you is, do you think that it is feasible to express a regulatory definition of what is an acceptable implant, not from a clinical view, but from a regulatory view, in terms of the percentage of source strength that is placed in the right organ?

DR. POTTER: I mean, that might be a good way to do it. I do think that there needs to be some degree of standardization. I know that some states are more onerous than others on how they define mis-administration. And to the degree that the NRC is capable of coming up with a definition, I think it would be helpful.

I sent out an email early this morning, although it's still preliminary in terms of what I would consider may be appropriate definitions, or appropriate ways to look at it. And one of those that I thought could be considered would be a reflection of the total isotope to volume relative to the prescribed dose. I

have a pretty good relationship with a lot of the vendors, and doing a lot of socio-economic work, I'm also involved in knowing how seeds are ordered by individual users. And there's a tremendous amount of variability where centers are ordering just what appears to be a tremendous amount of seeds for any one particular case. And if those centers were to be using all of those seeds in any one case, then that would represent a disparity of the original nomogram, which would represent the activity per volume. So the idea of a millicurie per cc relative to your prescribed dose within a certain range is something that may be available to use. And at the same time, the idea of calculating some degree of ratio of number of seeds within your PTV, your Planned Treatment Volume, relative to seeds that are outside of your Planned Treatment Volume may also be another way to come up with it without defining specific doses.

DR. MALMUD: Yes. That was, in fact, when the teleconference abruptly interrupted the last time, we were discussing just such a criteria, completely divorced from dose. And the proposal was to define both wrong site and I guess primary medical events in terms of the percentage of seeds prescribed that were actually

placed in a target volume.

DR. NAG: Hi, this is Dr. Nag. I think that toward the end of the last conference call we were within some type of agreement that if we can say that up to plus/minus 20 percent of the administered activity would be in the correct organ or the correct target. Now the major problem there is where is the target? I mean, let's say within the prostate you can see obviously the target is the prostate. Now which part of the prostate? Are you talking about the capsule, are you talking about two or three millimeters beyond the capsule? So again, how do you define exactly where the target is?

DR. SCHENIR: Well, Subir, I think that that's why you don't define it based on prostate. You define it based on a target volume. And for somebody like - Greg is not on the call, but Greg Merrick's philosophy of implanting is to define a margin around the prostate such that his Planned Treatment Volume represents the volume of the prostate plus two or three millimeters around the capsule of the prostate. And so, his criteria or his definition of a PTV is a little bit different than mine, which is pretty much to the capsule, plus maybe one, one-and-a-half millimeters of

margin around it. And so, to the same extent that with external beam, that the definitions for mis-administration are based on your planned target, and not an organ specifically, I think it would hold true to use the same approach because of that variability.

DR. NAG: But then again, you can artificially change your target. If you're allowed then to say I'm now expanding my target - let's say you make a mistake and you put double the quantity you were supposed to, you can just artificially increase the target and you'll still be within your limit.

DR. SCHENIR: Listen, there's opportunity to abuse any of these definitions, I think. And I know that for external beam there's additional opportunity to abuse these definitions. I think if a center's philosophy is to define the PTV based on a two millimeter margin around the capsule, and they have a case that appears to exceed that, and all of a sudden they change their PTV definition to three millimeters, or four millimeters against what their internal standard is, unless an inspector comes by to notice that and question it, you could probably sweep it under the carpet. But I think there's less variability or less subjectivity than there is with contouring and calculating

mis-administrations based on a d-90 dose or a v-100-type of dose.

DR. MALMUD: I think that Dr. Potter has brought a very good point up. Unless one unduly restricts the practice of medicine, it's probably not possible to create a foolproof system that some unethical practitioner couldn't get around by unfairly modifying the definitions for a specific case.

DR. SCHENIR: I mean, Subir, if you were to take your example - let's say process of care is I see a patient in my office. I do an ultrasound. I measure their prostate at 30 grams, and that's my volume that I'm calculating my order of seeds on. I'm calculating 30 gram prostate. I will order 30 millicuries of Iodine based on the nomograms. It's almost a one-to-one, and I usually half millicurie seeds, so I would order 60 seeds for that patient. Plus, because I'm doing realtime dosimetry in the operating room, I would probably order about an extra 10 percent or so, and round-off the even number. I would probably take 70 seeds to the OR with me. And my intent then is to implant a 30 gram prostate, so that if you were to define the activity for a prescribed dose of Iodine of 145 gray, and say that there is plus or minus 15 or 20 percent

activity allowed based on that initial calculation, and I go in there and I implant 80 millicuries, or 90 millicuries, and then at the end of the day I try and bumper it by recalculating my PTV after-the-fact, that's just not going to look too clean.

DR. NAG: I mean, I certainly agree with you, and I do the same way as you go with the realtime dosimetry and so forth. But the problem is then how do you catch the persons who have done the exact correct amount of millicuries, which in your case was 30 millicurie, but instead of putting it in the prostate --

DR. SCHENIR: Well, that's why by you --

DR. NAG: -- put those seeds into the penile bulb, and only 20 seeds into the prostate itself.

DR. SCHENIR: Well, that's why your definition has the word "and", so you do an activity per CC, and a PTV, number of seeds within the PTV; so that way it sort of freezes the abusers who then at the end of the day change their Planned Target Volume to a greater amount. You planned for 30, and so you have 60 seeds, and 40 of those seeds are outside of your Planned Target Volume, and so now you're stuck with your 30 gram Planned Target Volume. You can't go back and perhaps

change it, so that you can use -- just sort of thinking off the top of my head, you could probably use both definitions to sort of limit some of the subjectivity. Because if you just use one, then you say well, my Planned Target Volume in the OR changed from 30 grams to 40 grams. But then when I did my CT, or I did my post implant analysis, all the seeds were outside of the prostate anyway, so now I've just changed my Planned Target Volume to 50 grams. So you can sort of link them potentially, and that may eliminate some of the subjectivity.

DR. NAG: I think at the end of the last meeting or last conference call, that's basically what we came up with. One of the problems we were having is how do you then define what is the wrong site? I mean, it seems very simple. Anything outside your organs that you have defined is the wrong site. Okay. Then let's say your site is the prostate, you want a definition of the wrong site, so how do you define the wrong site?

DR. SCHENIR: Well, I think if you define the PTV as the prostate plus a volume, plus a margin, and that defines your PTV, then that's it. That's what you're calculating it on.

DR. WILLIAMSON: How large a margin would you recommend?

DR. SCHENIR: Anywhere from zero to three to four millimeters.

DR. NAG: That is only for the prostate. We also have to define it for any permanent implant. As you know, if you have a resection and many times you do an implant after resection, your target volume is the tumor bed, plus since there is really no organ, now we are implanting the tissue, which was the tumor bed, so you have to go beyond where your target was.

DR. SCHENIR: Well, no. There's a gross tumor volume, so there's a GTV that would represent whatever you're defining your treatment on. And then there's your Planned Target Volume, which represents your planned volume relative to the GTV. And so, if you make the definition on a Planned Treatment Volume, it would work for breast, it would work for a pancreas implant because you're now establishing a volume. You're establishing something that you want to treat, that you're defining your prescription to. And that incorporates your gross tumor, your organs, whatever you want, plus some extra margin or not, and the same thing sort of holds. You're still going to calculate

based on a prescribed dose, based on a volume, based on an activity, so I think it still holds.

DR. NAG: I know it holds, but how do you define wrong organ? The definition of mis-administration includes implantation of the wrong organ. How do you --

DR. SCHENIR: Well, how do you deal with external beam? I mean, if my tech treats a horizontal field laterally, you know, they turn a rectangle 90 degrees off, and now I'm exposing unplanned tissue, I mean that's outside of my prescribed dose, and that's outside of my prescribed Planned Treatment Volume, so can I hide that by going back and changing my prescription? Well, I'm not supposed to do that, so I think if you tie it back to what you're prescribing, I don't think there's really a problem with it.

DR. MALMUD: Well, I think Dr. Nag had in mind at the time he was speaking, remembering back to January 18th, there are cases where maybe only interoperatively can you define the target site. Perhaps you are treating some tumor bed that's exposed only at the moment of surgery, and so you plant all of these seeds in there, and in that sort of case, how would one ever adjudicate a claim that X percentage of the

seeds were not in the PTV? How would you define -- what would be the criterion for a seed being in the PTV for a post op case?

DR. SCHENIR: There is no radiographic marker of where the tumor is.

DR. NAG: There is no tumor because the tumor has been removed. You are now left with only a PTV. There is no GTV, there is no gross tumor. So, therefore, basically you have to then say that the area of the tumor bed, so what I normally do in these cases is when I prescribe, I say to the tumor bed. And really, there is no real way of confirming where exactly that tumor bed is. But so long as it's in the region of where the tumor was --

DR. SCHENIR: Well, you're always going to have that disparity. You have -- you treat an electron boost to the breast for the tumor bed in a patient who doesn't have a marker. And if you just treat the scar, a lot of these surgeons will tunnel for cosmetic reasons and stuff. I mean, how does anybody ever define your Planned Target Volume? So that I think we're never going to solve that. If you just keep going in that direction, you're never going to solve it. I think that everybody has the intent of treating a certain area, and

you define that intent in your prescription, regardless of whether there's a tumor or it's been ressected, or whatever it is, then that defines what you're going to be treating.

DR. MALMUD: This is Malmud. May I interrupt for a moment and try to refocus us. It is not the mission of ACMUI to establish practices and standards. It is our mission to deal with the public's exposure to radiation. And it sounds as if the administration of prostate bracheotherapy, or perhaps permanent seed implants, in general, is a very systemized method of precise estimates. And that these estimates fire a certain degree of flexibility with regard to establishing guidelines for the appropriate administration to the target organ, and to adjacent organs or tissue.

Current standards are probably adequate given the current technology. And from your earlier comments, Dr. Potter, you suggested that there are perhaps newer ways, and improved ways on the horizon for establishing and measuring the dosimetry. Now is that a fair summary of the state-of-the-art, Dr. Potter?

DR. POTTER: Yes. I think if you look around the country, I just don't know if there's that

much danger or damage that's necessarily being done. So in terms of trying to come up with a strict definition, it just doesn't - I'm not sure if I'm answering your question.

DR. MALMUD: You are answering my question.

DR. POTTER: I just don't know if (a), since there is some evolution of the procedure, if you create a definition based on the ACR standard of two to four weeks, and I'm about to publish a paper that says that I'm comfortable with my interoperative dosimetry, then that creates a burden on the future, I think, of where there is going. And in light of the fact that I'm not sure what the NRC records are, what they indicate in terms of really negligent, or really significant issues, it's not clear how onerous you need to create a definition at this time.

DR. MALMUD: Jeff, go ahead.

DR. WILLIAMSON: Yes. I'd just like to make a comment to explain to Dr. Potter one of the problems from our perspective.

There have been a series of really bad implants reported to the NRC where substantial fraction, more than 50 percent of the activity was

placed outside of the prostate in a wrong organ. And this, apparently, was discovered some time after the actual implantation. And what happened is that the practitioner simply revised the prescription to indicate that the seeds could be implanted in the rectum or wherever they happened to be. And this was very distressing to the NRC staff, as well as to the ACMUI when we were apprised, so our practical problem - and this was based on a suggestion again of Dr. Nag's January 18th - the practical problem is to come up with a simple enough definition of where the -- of a written directive, and what constitutes plus or minus 20 percent compliance with the written directive, so that at the time of the implant, during the interoperative procedure, the physician could be reasonably well-assured that the activity was where he thought he was, plus or minus 20 percent. And at that point, then it would be permissible to place in the rule a 24-hour limit on revising the prescription to prevent people from coming six months later and revising the prescription solely to avoid regulatory scrutiny.

The idea was could we, by an activity or source strength-based system, make it simple enough that some limitations on the revisability of the written

directive could be imposed without essentially constraining the legitimate practitioner in any way.

DR. POTTER: Well, to the degree that I'm aware of some of the ordering process for the seeds of physicians, and I'm not aware of some of the cases that have been reported to the NRC. It wouldn't surprise me that there are some sort of dangerous outliers.

To me, and I'm not part of the committee, and I'm not involved in writing the statutes and the language, but to me, I don't understand how anyone is allowed to go back and change any prescription once it's signed. So I think the standard should be that you prescribe and even -- here's something that's interesting in the sense that even though I'm doing realtime dosimetry in the operating room, I am still -- the computer that allows me to do that has built into it its definition of my PTV. I contour a prostate, it automatically calculates a 1-1/2 millimeter margin around that prostate, so that if I go into the operating room with the intent of treating a 30 gram prostate, and by the time I put the needles in and contour the prostate, it's now a 34 gram prostate for whatever particular reason, whatever variability existed in my measurement initially, versus the interoperative

measure, the computer is still going to calculate that with a certain PTV, or a certain margin that's calculated in, that still goes back to what my original prescription was.

DR. NAG: Dr. Nag. I think that's not the problem. I mean in instances where you can see the volume, you know the volume, interoperatively the volume has increased or decreased a little bit - none of those are problems. I think the major problem, that the reason why there was such major mis-administration was the person who was doing the ultrasound did not recognize which is prostate and which one -- what is bladder, so they thought that the bladder was probably the prostate. Everything looks black in a round thing there, and they contoured the bladder as being the volume they want to implant, and they put the seeds there. You see the problem there. It's not that -- and later he found that was not the prostate, that was the bladder that he contoured.

DR. POTTER: Well, then that represents -- listen, mistakes happen, and the concept of mis-administration is not -- obviously, it's a regulatory burden for anybody to have to deal with. But to the degree that mistakes happen with external beam,

with isotopes, with any sort of process, we're just trying to prevent that from happening by coming up with these rules.

If on any particular case it does happen that that's the case, then it's worthwhile that that patient understand that, in fact, that happened that way. Whoops, the bladder got treated. It wasn't our intent to do so, it wasn't prescribed, as such. I don't know. I'm not going to be converted based on that, but I think I'm going to have to step off the call, and I apologize for that, but I think some degree of activity of isotope relative to your prescribed dose, relative to your volume of PTV, however you define that, with some sort of an analysis, and that gets fixed in your prescription, that then is converted into some sort of analysis to show that 80 percent of your activity was within that PTV, probably makes some degree of sense without absolutely defining doses to normal tissues, or exactly how the doses should be within the prostate.

DR. NAG: I think I agree with that viewpoint. And, Dr. Malmud, just to clarify to the other people who may not have been on the conference call in January, it's basically immaterial whether you are doing the proposed implant dosimetry the same day or two

weeks later, or four weeks later. The ABS has that you can do it the day of, or within four to six weeks. That's not the problem.

I think from what we have heard today, if we define that a certain -- that the prescription of permanent implant being that a certain quantity or activity of the isotope be placed within a certain defined target, instead of saying organ, we can say target and leave it at that. If it's 20 percent more or less than that within the target, that will be a mis-administration.

DR. POTTER: Yes. Listen, again I apologize for having to step off the call. I'd be more than happy to address officially or unofficially by phone or email any additional questions that come up.

DR. MALMUD: Thank you, Dr. Potter. We appreciate your time and your having joined us on relatively short notice.

DR. WILLIAMSON: It was very helpful.

DR. POTTER: All right. Thank you.

DR. MALMUD: I think that this is very close to some of the positions we actually approved in the January 18th teleconference prior to coming to loggerheads over the definition, I think, of wrong site

was where we stopped.

DR. WILLIAMSON: Yes, I think -- if I may, Jeff, I think part of the concern was among some of the members who are not familiar with the practice of radiation oncology, and were concerned about the retroactive changing of the written order in the light of the outcome of the therapy. And there was, I suspect - no one said this openly, but I suspect there was concern that perhaps there was too much flexibility in changing prescriptions with regard to what actually occurs. And that the concern was that something might be done which was not in the best interest of the patient.

It seems to me having heard some of the descriptions today about the practice of radiation oncology, that there are sound reasons for this. The change in the anatomy after the administration, the swelling as a result of the administration, and that the timing of the dosimetry is, in fact, a currently accepted standard.

DR. MALMUD: I think that's correct. And by the way, this was, I believe, one of the consensus positions that survived from the January 18th meeting. I'll read to you from the summary, that essentially the

subcommittee thought that applying the 20 percent rule to a dose-based end-point was impractical as a regulatory criterion precisely for all of these subjective reasons. And it's so complicated and so subjective that it would be totally impossible with a dose-based system to place practical limits on when the radiation oncologist could revise the directive. And I think that while I had some initial reservations, I think the ingenuity of Dr. Nag's suggestion that we look at a geometric criterion, what percentage of the seeds are in the target volume, what percentage are not in the target volume, et cetera, that is simple enough that in many cases like prostate, it's more readily definable. And it's simple enough that in an interoperative setting, a good physician ought to be able to know, have confidence where the seeds are, and so can write a final revision within 24-hours of the implant, making this type of restriction possible.

DR. WILLIAMSON: I'm not sure that within 24-hours of the implant is the agreement that we had then. It was a concern then, but not an agreement. Am I --

DR. MALMUD: That's absolutely correct. We did not agree on -- we could not agree on placing

limits on the length of time for revising even activity-based prescription.

MR. LIETO: Excuse me. This is Ralph Lieto. No, that's not true. Our agreed upon recommendation if you look at the transcript, states that for permanent implants, we agreed that the completion of the written directive and documentation would occur within one working day of source implantation or insertion, so we did agreed upon that. And I think based on what Dr. Potter was also stating, he didn't seem to have problems with that either. In fact, he kind of almost sounded like when you leave the OR, you should have made any changes at that time. But I think within a working day gives, I think, a lot of flexibility to practicing bracheotherapy radiation oncologists.

DR. NAG: This is Dr. Nag. Actually, you would know by the time you finish the implant. The reason for putting the 24-hours or one working day is to be consistent with the rest of bracheotherapy. For example, in Iridium bracheotherapy or low-dose rate bracheotherapy, all of that is that the revision, if it's revised, has to be within one working day, so it's just to be consistent that the one working day was

placed.

DR. WILLIAMSON: Yes. I do have that in my January 13th Minutes, revised summary, revisted on January 18th, that we had agreed upon that. I wasn't sure that it survived the last committee meeting on the 18th.

DR. MALMUD: I believe that the 24-hours was discussed. I said that I thought it should be a working day, because what would happen if this happens on a Friday? So does anyone wish to make a motion at this point with regard to the working day?

MR. LIETO: Dr. Malmud, this is Ralph Lieto. I don't think we need to. I mean, if you -- not that I read the Minutes and the transcript, but if you look at page 71, I believe it is, that's where we agreed and voted on it as a committee, that it was one working day, not 24-hours.

DR. MALMUD: Okay. And the purpose of today's discussion was to make sure that we weren't doing something that was unnecessarily restrictive of the practice of medicine, and create unintended consequences.

DR. WILLIAMSON: Dr. Malmud, this is Jeff Williamson. May I make a comment about this?

DR. MALMUD: Please, do.

DR. WILLIAMSON: I think it is premature to make a recommendation on restricting the authorized user's ability to revise the written directive until we have come to agreement what is the criterion for a wrong site and medical event itself, because if you allowed dose-base written directives, this would unfairly penalize those who do post implant dosimetry, and would choose to continue writing their written directive that way. So I really think it's a matter of putting the cart in front of the horse to --

DR. NAG: Hi, this is Dr. Nag. I think we have already agreed that we are not doing this as a dose-base. It will be activity-base. That has already been decided, and that has been confirmed and written in the Minutes, so why are we going back now to dose-base?

DR. WILLIAMSON: I think we better review the recommendations we agreed upon and make sure that in light of the additional information and the abruptness of the termination of our last phone conference, we all agree that this is a reasonable body of recommendations to present. That's what I'd suggest and see if they're all consistent with one

another.

MR. LIETO: This is Ralph Lieto. Jeff, then are you asking that we then go back to our specific recommendations from the January meeting and re-address where we left off?

DR. WILLIAMSON: I think we should at least summarize the recommendations that we believe we all voted for, yes.

DR. NAG: Okay. This is Dr. Nag. May I make a motion or suggestion that for the purpose of mis-administration, we define permanent bracheotherapy, the written directive be written in terms of quantity of activity in site as millicurie, that they're to be implanted within a target volume, any revision, if required, is to be made within one working day of the implant procedure.

DR. MALMUD: Is there a second to that motion?

DR. WILLIAMSON: What is the criterion for a medical event? It's not mis-administration any more, it's medical event.

DR. NAG: Yes. Medical event would mean plus or minus 20 percent of the intended activity. And in addition, we have to add that any activity that was

implanted within the target volume but subsequently migrated to other organ, that would not constitute the mis-administration.

DR. WILLIAMSON: Do you agree that that proposal is equivalent to the following one in our summary: "Any implant is a medical event if (a), the total source strength implanted anywhere in the patient exceeds the written directive by more than 20 percent, or the total source strength implanted in the target volume deviates from the written directive by more than 20 percent."

DR. NAG: No, I think only the second part, not the first part.

DR. WILLIAMSON: So you would agree it's okay for a practitioner to write a written directive to implant 100 millicuries into target volume, and implant another 100 millicuries in some wrong place next to the target volume. You agree that's not a medical event?

DR. NAG: No, but the medical event was that they intended to put a certain volume within the target. And if they put in that volume, they put in the number of activity within that volume, then they are within -- it's not a mis-administration. Now if they have put additional amounts in a different area, then

it comes under the definition of implantation of the wrong site.

DR. WILLIAMSON: So the definition I read you was intended to cover both the wrong site, as well as the correct treatment of the target volume itself. But do you agree there should be a wrong site criterion based on activity for the entire medical event rule?

DR. NAG: Well, then it becomes -- I don't think I'm getting it. If you put in 200 millicuries, you want just to put 100 millicurie within a volume. Okay. Now you are putting in 200 millicurie, 100 of which is inside the volume, and 100 of which is outside the volume.

DR. WILLIAMSON: Yes.

DR. NAG: So now you have put in 200 millicurie, so you have revised to say that you are now putting in 200 millicurie, so in that case only 100 millicurie within the volume, so it will become a mis-administration.

DR. WILLIAMSON: So according to your statement -- I'm sorry to debate what must sound like an archaean technical point, but according to the proposal you made it's a medical event if the amount of activity that gets into the target volume is within plus

or minus 20 percent of the prescribed activity, I'm just pointing out an obvious counter-example to that. If that's the sole definition of medical event, I guess what I'm posing to the group as a counter-example, that you need an additional clause that restricts the amount of activity relative to the original written directive that can be placed in extra target tissue, and that's why in this definition I read, it had two clauses, one which functions as essentially the same as Dr. Nag proposed, and the other would declare an implant to be a medical event if the total activity placed in the patient during the procedure exceeds by 20 percent.

DR. NAG: I'm sorry. The way we --

DR. MALMUD: Gentlemen, I understand the point that you're making. I think that most of the members of the committee understand the point.

Dr. Diamond, are you still on the call?

DR. DIAMOND: Yes. I just came back five minutes ago from being pulled off for a patient.

DR. MALMUD: Okay. The question before the committee that Drs. Williamson and Nag are discussing is whether or not the amount of activity, which we are discussing, not the therapeutic dose, but the amount of activity administered - let's say the

prostate is being treated, and the goal is to put 100 millicuries in. Instead, what happens is that the therapist recognizes halfway through the procedure that 40 millicuries has gone into the bladder. The therapist now administers 100 millicuries to the prostate, but 40 millicuries is now in the bladder, or in other tissue, in tissue other than the prostate. Is that considered a mis-administration, because the prostate has gotten the right dose finally of 100 millicuries, plus or minus zero, but that the bladder has gotten 40 millicuries which was unintended in toto. Should that be considered a mis-administration?

DR. DIAMOND: If I understand your example correctly, Leon, the intent was to deliver certain activity to the prostate, but because of, for example, operator error, that 40 percent of that was actually delivered into the bladder itself, missing the target of interest. Is that correct?

DR. MALMUD: Yes. And then an additional 40 was administered into the prostate, so that the prostate did get the right therapeutic dose finally, but only after 140 millicuries was administered.

DR. DIAMOND: I see. So in realtime or immediately post facto, an additional 40 millicurie was

placed into the target organ to bring it up to the desired result. Is that correct?

DR. MALMUD: Correct. Now the question is, shall that 40 millicuries which went astray into the bladder and was identified as going astray into the bladder during the therapeutic process, should that be considered a medical event?

DR. NAG: This is Dr. Nag. Before we go further --

DR. WILLIAMSON: Let him finish.

DR. DIAMOND: To answer the question, I would say yes; in this particular case of the 100 millicurie intended for the prostate, fully 40 millicuries were geographically distinct - in other words, this is not a peripheral loading of a prostate implant. This is actually seeds going some distance away into the wall, the bladder, deep, retained within the bladder itself, into the rectum, for example - at that magnitude, I would say the answer is yes.

DR. NAG: Okay. This is Dr. Nag. Dr. Williamson, I think in this case it is the prescription if you're under 100, you have put 140 millicurie, so automatically your prescription if you're revising it will have to be 140 millicurie, 100 millicurie has gone

into the prostate so it is more than 20 percent.

DR. MALMUD: Well, Dr. Nag, in the example that I cited of a prescription for 100 to the prostate, and discovering early in the course of administration that 40 millicuries has gone into the bladder, that there was an additional 40 millicuries available so that the patient did get 100 to the prostate.

DR. NAG: Right.

DR. MALMUD: The total amount given was 140, but 40 of it went into the bladder. Would you report that as a medical event?

DR. NAG: Yes, it would be.

DR. MALMUD: It would be.

DR. NAG: Sure.

DR. MALMUD: Dr. Williamson.

DR. WILLIAMSON: Yes.

DR. MALMUD: So Dr. Nag agrees in principle with the point that you are making.

DR. WILLIAMSON: Yes.

DR. MALMUD: Would you care to craft the words that you think would cover a situation such as that, as a motion?

DR. WILLIAMSON: Yes. I propose the following definition of medical event. "Any implant is

a medical event if (a), the total source strength implanted in the patient exceeds the written directive by more than 20 percent, or the total source strength implanted in the target volume deviates from the written directive by more than 20 percent."

DR. MALMUD: Is there a second to that motion? Then we'll have some --

DR. NAG: I object to that, because the second definition will automatically cover the first definition, because now you have given more than your 20 percent, so you only need to state your second definition, that the amount that you are prescribing is plus or minus 20 percent within your target volume. That's all you require, but the other will automatically be included, because if you are giving 20 percent extra seeds, that is 20 percent more than what you intended.

MR. LIETO: I think the problem from my perspective is an issue with language and the logic of the definition. Since the written directive really directs that seeds go only into the prostate, in fact, the 40 millicuries is not prescribed at all, so there's no way --

DR. NAG: Right. If it's not prescribed, how could it have been placed there? So anything you're

putting in is within that volume. That means that that person is not saying it's not prescribed, that means we are putting in an activity that was not even prescribed, so that automatically becomes a mis-administration.

DR. WILLIAMSON: This is why the original medical event definition as it's now on the books had two provisions. It had a provision for a primary definition, which was based on the accuracy with which the target dose is achieved, and then it had a second provision which precluded you from basically implanting other areas other than the target volume, so I guess my legal claim or argument is that in order for the medical event definition to be complete relative to the definition of written directive, our proposal must also have two equivalent provisions.

DR. MALMUD: Dr. Williamson.

DR. WILLIAMSON: Yes, sir.

DR. MALMUD: Do you feel that the current wording is inadequate and needs to be changed at all?

DR. WILLIAMSON: Yes, I do, Dr. Malmud, for exactly the same reason that Dr. Nag has repeated in earlier meetings, and Dr. Potter so eloquently re-expressed to us; that is, that the dosimetric criterion is too subjective, and there's too much

legitimate medical variability in how the target volume and dose distribution is assessed.

DR. MALMUD: Thank you. I just wanted to make certain that you were still on the same page.

DR. WILLIAMSON: I believe that this is an opportunity to make a significant improvement to this regulation, which I think is unduly complex. And as Dr. Nag has stated earlier, some parts of it are clearly unenforceable, and would lead to ridiculous consequences if they were looked at in detail.

DR. MALMUD: So the changes that you and Dr. Nag are recommending are to move from a dose-based to an activity-based criterion.

DR. WILLIAMSON: That is correct, or within the domain of permanent implant, at least.

DR. MALMUD: Yes. And to maintain the 20 percent cap, and to define more clearly how the 20 percent is described.

DR. WILLIAMSON: That's correct.

DR. NAG: And I think that's agreed by all of us who have expressed their opinion so far.

DR. MALMUD: So in terms of principle, we agree it's simply a matter of crafting the words.

DR. WILLIAMSON: That's correct. And

this is exactly where the conversation broke down last time. And as I recall, Dr. Nag felt that the dosing wrong site criterion that's on the books now was acceptable, and I thought it's inconsistent with the whole philosophy that we've been proposing of trying to simplify the system and make it more workable. But I really do believe a wrong site criterion is needed for the medical event to have any teeth, or to capture wrong site medical event.

DR. MALMUD: Now you have made a motion, and we were looking for a second, but Dr. Nag had another comment. Is there yet a second for Dr. Williamson's motion? Is there no one who wishes to --

DR. DIAMOND: Yes, this is Dr. Diamond. I would second Dr. Williamson's motion.

DR. MALMUD: All right. The motion has been moved and seconded by Dr. Williamson and Dr. Diamond. Is there any discussion of that motion at this point?

DR. NAG: Again, I think I wish to reiterate that we don't need two points. One point would cover both of them.

DR. ZELAC: Dr. Malmud.

DR. MALMUD: Yes.

DR. ZELAC: This is Dr. Zelac. I have a question before you proceed.

DR. MALMUD: Yes, Dr. Zelac.

DR. ZELAC: Is this a vote of the subcommittee?

DR. MALMUD: Yes, it is.

DR. ZELAC: Okay. And secondly, I'd like just to remind everyone that our Office of General Counsel has in the past determined that there is equivalence between total source strength, i.e., the activity, and total dose. So in terms of the existing wording for written directives, the after implantation portion gives both of those total source strength or the total dose, but the pre-implantation requirement for information is only couched in terms of dose. And that, I think, is perhaps where part of the problem is; that the individual physician might initially be creating the written directive in terms of dose, and then make a decision later to simply report the total source strength implanted instead of it. So I think we're moving in the direction of getting where we want to be, but I wanted simply to remind that we do have already in the existing rules, both for written directives and for medical events, equivalents of total source

strength and total dose.

DR. MALMUD: Thank you, Dr. Zelac, for clarifying that. Dr. Williamson, do you wish to comment on it?

DR. WILLIAMSON: I do. I believe that Dr. Zelac is correct, that essentially Dr. Nag's proposal and half of my proposal are consistent with the rules that are already on the books. This is basically addressing the possibility of defining medical event with respect to target volume accuracy in terms of plus or minus 20 percent of the intended activity being delivered.

However, if one reads carefully the wrong site definition, one sees that it is really based on absorbed dose terminology, and I don't believe that the way the rule is written now, that could ever be interpreted in terms of implanted activity.

DR. DIAMOND: I agree.

DR. WILLIAMSON: So I believe that a fix is necessary. First of all, if a 24-hour revision is going to be -- I mean, a one working day revision limitation is going to be plausible, the whole system has to be simplified, because if you allow dose-based prescription to continue, you have to let those people

have an out for 30, or 60, or whatever number of days they want based on their clinical practice. But if you say everybody is going to use implanted activity, both for the wrong site criteria and the accuracy of delivery to the target volume, then I think you have a chance of making a one-day restriction palatable to the community.

DR. MALMUD: I think your point is well made with regard to the compliance within the one working day being more easily related to activity-based calculation, than dose-based.

Dr. Nag, would you care to comment on that?

DR. NAG: Yes. I have one comment on Dr. Zelac's statement. Even as written, even before the implant a written directive will allow you to write either total dose or activity, so even now my intended method of writing my directive for permanent implant is to state I'm intending to give so many millicuries.

DR. ZELAC: Well, let me just comment that if you look at the wording specifically, the information required before implantation is treatment site, the radionuclide and dose. Now because of the OGC ruling, one could interpret dose as meaning total source strength, or total activity, the actual words in the

rule are only dose, and nothing to do with activity.

DR. NAG: In one place it's the dose, in the other place, if you look at other places within the 10 CRF 35, another place would say dose or activity, so I don't have the 10 CRF 35 with me right now, but I have gone over that, and we have discussed that before, that in some places it has written dose, and I'm sure that is what you're commenting on. But in other sections under written directive it allows you to say all activity.

DR. ZELAC: Just for clarification, what I was referring to is, in fact, the written directive requirements for permanent implant bracheotherapy and other similar bracheotherapies, low, medium, and pulse dose rate, and only excluded high dose; so the words in the rule for that which would apply to preparation of a written directive for permanent implant bracheotherapy says treatment site, radionuclide, and dose as the required information.

DR. MALMUD: Thank you for clarifying that, Dr. Zelac. Dr. Williamson has a motion which has been seconded. Is there any further discussion of Dr. Williamson's motion?

MR. LIETO: Yes. This is Ralph Lieto.

DR. MALMUD: Yes, Ralph.

MR. LIETO: Jeff, is your statement on the medical event definition, is that one of the recommendations in the report from January?

DR. WILLIAMSON: Yes, it is. I will point out that this requires -- for this recommendation to be plausible, it implies that permanent implants need to be exempted from the current wrong site provision of the medical event definition.

MR. LIETO: Well, I guess I have a little bit of a problem with that, because I got the impression from Dr. Potter's presentation that using an activity-based written directive, that if it was defined in terms of the PTV, that Planned Target Volume, that you still could reasonably establish a wrong site criterion for permanent implant.

DR. WILLIAMSON: Yes, I think he agreed. My understanding is that he agreed basically with the philosophy of the motion that's on the table.

MR. LIETO: But you're saying that your definition would require exempting.

DR. WILLIAMSON: The Provision A in the recommendation that I read replaces the current medical event wrong site criterion for permanent seed implant.

So an implant is a medical event if the total source strength implanted anywhere in the patient exceeds the written directive by more than 20 percent, or the total source strength implanted in the target volume deviates from the written directive by more than 20 percent. So either under or over-dosing the target by 20 percent, or putting 20 percent more seeds somewhere else in the body would trigger medical event, and have the functional equivalent or counterpart of the current wrong site provision. That's the idea.

MR. LIETO: So just a point of clarification; when you say "target volume", and Dr. Potter is talking Planned Target Volume, are we essentially saying the same thing?

DR. WILLIAMSON: Yes. I use the term in exactly the same way he meant. This is part of the polishing of the language to figure out what is a good way to describe that, but it essentially means the volume that the practitioner intends to deliver the seeds inside of.

DR. MALMUD: Now may I ask a question while we're on the table, Jeff, what happens in a situation where the MRI or CT cannot be done within one working day of the administration of the bracheotherapy and,

therefore, the calculations which are most accurate may occur at some time later?

DR. WILLIAMSON: I think another assumption of this proposal is that based on the either operative exposure of the target's volume, say a tumor bed, or intraoperative imaging as it's now practiced using ultrasound for prostate, this determination which is very simple, are the seeds in the planning target volume or not, could be made within the plus or minus 20 percent tolerance level by a competent practitioner.

DR. MALMUD: I would now address Dr. Williamson's point, if I may as Chair, to the two therapists. Is that practical in terms of your daily practice of radiation oncology?

DR. NAG: Dr. Nag. Yes, I mean it's practical. But I mean, we've always had a planned target. It's immaterial whether you are doing a post implant dosimetry one month later, two months later, or the same day. I mean, that's immaterial.

DR. MALMUD: Okay.

DR. DIAMOND: I agree, that's practicable.

DR. MALMUD: All right. So do we feel ready to move on the motion?

DR. NAG: Before you do that, I would just

like to add one point to the motion, and that is if a certain activity has been implanted within the target volume, but there has been a subsequent migration of situs of this volume, which is no fault of the patient or the implanter, that quantity should not be included within that mis-administration definition. For example, if you implanted 100 millicurie within the target volume and 10 of those seeds went to the lung later, that 10 seeds would not be counted. And that provision is there at present in 10 CFR 35, and a wording similar to that has to be included in any new definition.

DR. MALMUD: Dr. Williamson, are you willing to amend yours?

DR. WILLIAMSON: Well, I agree that it should be included. Whether you want to add it to this motion; this is what I've been trying to say. The whole thing has to be crafted in one piece so we can see that all the required components are there, but I fully agree with Dr. Nag that seed migration and patient intervention and other things should continue to be exempted from the medical event definition, as they are in the current rule.

DR. MALMUD: May we accept that as a one-line amendment to your motion, Dr. Williamson?

DR. WILLIAMSON: Sure.

DR. MALMUD: Thank you. Dr. Nag, will you second that motion?

DR. NAG: Yes.

DR. MALMUD: Thank you. There is an amendment to Dr. Williamson's motion, and it has been seconded by Dr. Nag. If there's no further discussion, may we move on that motion?

MR. LIETO: Well, this is Ralph Lieto. Why do we need to include it if we've already in our previous meeting included that in the definition of a written directive?

DR. NAG: Ralph, we are making now a new motion? This is included --

MR. LIETO: This doesn't change the previous approved recommendation. This is a different recommendation all together.

DR. WILLIAMSON: I think the best thing to do is assume that it supersedes earlier approved motions that are very similar but subtly different from this one.

DR. MALMUD: Are you willing to accept that, Ralph?

MR. LIETO: I've got some real problem,

that we're just making all these changes, and it's like we're starting all over, and the January meeting didn't exist.

DR. NAG: No, no, no, no.

MR. LIETO: I mean, if we're sticking with just this recommendation, which is a separate recommendation that we didn't address in January, which is on page 6 of the subcommittee report, that's fine. I don't have any problems with that. But we're making all these additions and changes as if we're ignoring the previous work that's been done.

DR. MALMUD: But may I ask you a question, Ralph? Which do you think is the clearer of the two motions, the one from January or the current one?

MR. LIETO: The one before the addition of the -- the add-on addition, the original proposal motion by Jeff that was seconded. That one I think is clear and succinct, and --

DR. MALMUD: You think that the point about the migration is unnecessary.

MR. LIETO: I do.

DR. NAG: I have strong objection there because what will finally come out is that the points, and then someone will say well, now the seeds migrated

after that, but that is not considered.

MR. LIETO: We're already on record as saying that seed migration is excluded. We've already agreed we're going to recraft what we're recommending into a single revised document for the committee to look at.

DR. WILLIAMSON: Dr. Malmud.

DR. MALMUD: Yes, sir, Dr. Williamson.

DR. WILLIAMSON: May I make a comment? We already said in this 18th January, 2005 report that we agreed upon this. I believe that what happened during the January 13th meeting is because senses became unraveled exactly over the issue that Dr. Nag and I have continued to debate, which was the necessity of having some form wrong site medical event provision, so I especially disagree with Ralph. I think it is helping push the consensus process forward if we can vote on this motion, since we have seem to come within striking distance of a consensus on this very contentious point.

MS. SCHWARZ: Dr. Malmud, this is Sally Schwarz.

DR. MALMUD: Yes.

MS. SCHWARZ: I do agree that at least at this point considering that this is rather a

continuation since January, this finally is putting all the pieces together, and that as a subcommittee we could perform the vote today on all the pieces at a single time.

DR. MALMUD: Thank you, Sally. Now we do have a motion on the floor which has been amended. We've heard Ralph's objection to it.

MR. SULEIMAN: Dr. Malmud, Orhan. I'm back on again.

DR. MALMUD: Yes, Orhan.

DR. SULEIMAN: What's the motion that's on the floor?

DR. MALMUD: Jeff, if you would repeat the motion with the amendment so that Dr. Suleiman can hear it, as well.

DR. WILLIAMSON: Okay. Any implant is a medical event, excluding seed migration that is no fault of the practitioner, if (a) the total source strength implanted anywhere in the patient exceeds the written directive by more than 20 percent; or (b), the total source strength implanted in the target volume deviates from the written directive by more than 20 percent.

DR. MALMUD: Thank you. That's the motion. Dr. Suleiman, is that clear for you?

DR. SULEIMAN: Eighty percent was.

DR. MALMUD: Okay. Any further discussion of the motion?

DR. VETTER: This is Dick Vetter, just to clarify who's voting on this motion?

DR. MALMUD: The members of the subcommittee, and they are Dr. Nag, Dr. Williamson, Mr. Lieto, Dr. Schwarz, Dr. Malmud, Dr. Suleiman.

MR. LIETO: I think Dr. Diamond is on this too, isn't he?

DR. MALMUD: I haven't finished reading the list. Dr. Diamond, and I think that's it. Oh, Dr. Eggli, and Dr. Vetter, and Mr. Bailey.

MR. LIETO: Sounds like a committee of the whole subcommittee.

DR. MALMUD: Well, it's a large subcommittee, but it is a subcommittee.

MR. LIETO: I guess I'm confused now. Is this the subcommittee that --

DR. MALMUD: Only subcommittee today. You are a subcommittee, and it was announced in the record as a subcommittee.

DR. WILLIAMSON: Well, I think that Dr. Malmud has expanded the membership of our subcommittee.

DR. MALMUD: Excuse me for expanding the membership. Maybe Mr. Essig can clarify it for us. He always has been a good resource.

DR. ZELAC: Dr. Malmud.

DR. MALMUD: Yes, sir.

DR. ZELAC: This is Dr. Zelac. Unfortunately, Mr. Essig is no longer with us. He was drawn into another meeting. My recollection personally is that the subcommittee had a smaller membership. I'm not sure that necessarily it was limited to the view that participated in the past teleconference, but I think it was not as expanded as you have indicated.

DR. MALMUD: You're probably correct.

DR. WILLIAMSON: Acting as the apparently ex-subcommittee chair, I surely have no objection to these additional members. The more the merrier.

DR. MALMUD: May we call the vote? Are there any objections to the motion? I do want to vote today.

DR. SULEIMAN: Read the first clause of it again.

DR. WILLIAMSON: Shall I read it again?

DR. SULEIMAN: Yes, sorry.

DR. WILLIAMSON: Okay. Any implant, excluding seed migration, is a medical event if (a) the total source strength implanted anywhere in the patient exceeds the written directive by more than 20 percent; or (b), the total source strength implanted in the target volume deviates from the written directive by more than 20 percent. This is intended to cover both the situation where activity or a large portion of the activity is egregiously or erroneously implanted in some other volume, as well as the accuracy of delivery to the target volume.

DR. MALMUD: Thank you. All in favor? Any opposed? Any abstentions?

(Vote taken.)

DR. MALMUD: It is a unanimous motion. I thank you, ladies and gentlemen, for the yeomen's effort on behalf of -- now, is there any other business that this committee wishes to engage in at this time?

DR. BAILEY: Dr. Malmud, this is Ed Bailey. Are we now going to vote as a committee on the motion we just unanimously approved as a subcommittee?

DR. MALMUD: Actually, we could, could we not?

DR. WILLIAMSON: Dr. Malmud.

DR. MALMUD: Yes, sir.

DR. WILLIAMSON: May I make a suggestion?

DR. MALMUD: Yes, Dr. Williamson, suggestions are always welcome.

DR. WILLIAMSON: Okay. I believe this is a very complicated rule. I believe that it would be prudent for us to try to pull all of the pieces together in terms of a more comprehensive rough draft of rule language and study this at our face-to-face meeting and fine tune any provisions that need to be fine tuned before signing off on it formally as a committee.

DR. MALMUD: So you wish to defer this to the Full Committee Meeting in April in Rockville.

DR. WILLIAMSON: That's right. And I would like to have maybe an opportunity to try to embed this language in the existing rule language so it's clear what provisions would have to be modified, so that a rulemaking initiative, at least the implications of it are clear. It's a complicated rule. I would also --

DR. MALMUD: Dr. Williamson, I would only disagree with you on one point.

DR. WILLIAMSON: Yes.

DR. MALMUD: You have been so clear in your

drafting of the words, that even I understand it, so it couldn't be terribly complicated. Other than that, is there agreement that we'll defer this to the meeting in April among the group?

MS. SCHWARZ: Yes.

DR. NAG: Hi. This is Dr. Nag. I believe what I would like is to have the wording maybe - not the whole transcript, just the wording of those two sentences given to all of us.

DR. MALMUD: Dr. Nag, I'll ask Dr. Williamson if he would email that to us.

MS. SCHWARZ: I think that's an excellent idea.

DR. WILLIAMSON: You would like me to make a summary statement of what we voted on and reaffirmed today.

DR. MALMUD: Yes, as brief as possible, and just email it to all the members.

DR. NAG: I know the intention, but the language seems a little clumsy, and I want to sort of play around with the words a little bit.

DR. MALMUD: I understand. We will look forward to your comments, as well.

DR. WILLIAMSON: Well, I think that -- yes.

Anyway, I also think this is a major enough shift, it would be prudent for us to also hear what the community has to say about this matter. This is a large change in this rule.

DR. MALMUD: Yes. Are there any comments, by the way, from the members of the public who are with us today? That's Lynn Fairobent, Marten, Gonzalez, AWPM, ASTRO, ACR, S&M, any comments?

(No comments.)

DR. MALMUD: Thank you very much. Are there comments from staff? Dr. Zelac.

DR. ZELAC: No comments at this point.

DR. NAG: This is Dr. Nag. I would like to take this statement because the American Bracheotherapy Society board meeting is two weeks from now, and there will be at least eight practitioners of prostate bracheotherapy at that, and I can give some informal feedback from that at the April meeting.

DR. MALMUD: Thank you. We will look forward to that feedback at the April meeting. Any other business that this committee wishes to engage in at this time within the framework that was described?

MR. LIETO: Dr. Malmud.

DR. MALMUD: Yes, sir. This is Ralph

Lieto.

MR. LIETO: I can't hear too well because it sounds like something is breathing into the phone pretty heavily, but I don't know. Anyhow, I'm a little confused about our future course of action in terms of the subcommittee report made in January, is the intent that we are going to take what we did today with what we did in January, amalgamate that together, and then present that to the committee for their review, comment, and approval?

DR. MALMUD: Yes, that's correct.

MR. LIETO: There were some recommendations that have not been addressed that were in that report.

DR. MALMUD: Do you wish to bring any before the subcommittee right now?

MR. LIETO: Well, I'll first defer to the subcommittee chair, Dr. Williamson.

DR. WILLIAMSON: I didn't know I was still the subcommittee chair.

MR. LIETO: I didn't know you weren't.

DR. MALMUD: Dr. Williamson.

DR. WILLIAMSON: Let's see. Let me go through here. We've had such a contentious set of

meetings, it's difficult for me to actually recall what remains of the consensus, but I think we -- one area that is not resolved is the compulsory reporting of the medical event to the patient, or a member of the patient's family, regardless of the medical consequences of making this report to the patient. So this was, I still believe, a deficiency of the existing rule that a clinician who believes informing the patient of a medically insignificant medical event will harm the patient by upsetting them, or if they're not mentally competent, or for whatever reason, they are forced into making a -- a dilemma is imposed on them where either they have to violate the patient's confidentiality by informing a friend or relative that they randomly pick out, or they have to tell the patient anyway against their own medical judgment, so I believe that taking an opportunity to revise that aspect of the rule while we're at it, or recommending revision of that aspect of the rule would be indicated; but we have not, as far as I can recall, come to complete consensus on that. We were going to come back to that.

I think the other issues is the 20 percent absorbed dose threshold reasonable. We've come to consensus on that, and I don't think anything that's

been said subsequently -- there's a bit of polishing to be done here on this report.

I guess the question is for the Chairman, do you really want a big report like this, or should I just write this little one-page summary with maybe an expanded rule language, and let the staff come up with a rationale to submit to the commission?

DR. MALMUD: I think in general one-page summaries are preferred. They tend to be read, whereas, longer documents often are not.

DR. WILLIAMSON: We have not really -- one of the goals, or one of our assigned deliverables from the commission is how can risk associated with medical events, if any, be better conveyed to the public. I found this mission assigned to us by the commission very vague. I do not know what they mean, but as far as I know, we haven't really made any progress on that.

DR. MALMUD: Very often the best means of approaching a medical event, other than the prevention of one, is to make it clear to the patient during the informed consent process that these kinds of events can occur, and may occur in the treatment of the individual patient. Then when it does occur, the patient has been, number one, informed of the risk of it in advance; and

number two, is less panicked with regard to the event, since it was explained this might occur in the course of the treatment.

DR. WILLIAMSON: I believe one recommendation that has not been abrogated that's part of this, or I put under this, not really understanding what the commissioners meant. The subcommittee recommended that NRC staff strive to make the ME reporting process more like that of the regulatory community's own QA practice of follow-up, and QA practice review that occurs following detection of a delivery error or potential area, and essentially try to make it less of a punitive exercise.

DR. MALMUD: That is a superb recommendation.

DR. WILLIAMSON: So that's it. I don't know if anyone has any insight into what we were expected to respond to on behalf of the commission.

DR. MALMUD: I think that they we have responded. We have a motion, which when finally crafted together with the input of the extensive effort put forth in January, will be a document which the whole committee will be able to review and hopefully move on.

DR. WILLIAMSON: Okay. So I guess what I

will try to do is create the one-page summary of what I think the technical content of today's recommendations are by the end of the week. I will try to update this longer report, and take a look at the rule language, which is dispersed in three or four places throughout Part 35, and provide an additional report to the ACMUI in April about the consequences of these proposed regulations in terms of the need to wordsmith other regulations and definitions in Part 35.

DR. MALMUD: Thank you. Are there any other items that anyone wishes to discuss right now? If not, is there a motion for adjournment?

DR. NAG: So moved.

DR. MALMUD: There's a motion for adjournment, and I would just interrupt the motion for adjournment by wanting to thank each of you who has given so much of his or her time and thought to this process to come up with a final recommendation. It's quite obvious in listening to you that each of you is very concerned about the welfare of the patient first, and about what the implications are of each of the actions that we're taking with regard to patient welfare physically, as well as emotionally. And I want to thank each of you for the extensive effort, and the time. And

with that, we will call the meeting to a halt, and it is approximately 3:15 eastern time, and thank you all.

(Whereupon, the proceedings in the above-entitled matter went off the record at 3:17 p.m.)