

I'd like to say good morning to everybody and welcome to this continuing education course, Quality Assurance and Clinical Trials, A Primer for Physicists. I'm Art Olch from the University of Southern California and Children's Hospital, Los Angeles. This talk is a derivative of a new AAPM report of the same title which should be coming out in the next couple months and is the product of the Subcommittee on Quality Assurance Physics for Cooperative Trials of the Radiation Therapy Committee of the AAPM. Before I begin I wanted to just recognize the members, consultants and reviewers for the primer document. If you see any of these people at the meeting please go up to them and congratulate them on a job well done. One of the motivations for this talk and the report is that you don't generally find information on clinical trials in general or quality assurance physics in clinical trials, in particular in the curriculum for medical physics training programs. We felt that there was a lack of information in our

community and so we hope to fill that void. So this morning we're going to talk about some basic principles of what constitutes a clinical trial, and the role of the physicist in preparing and maintaining the institution's credentials for participating in our clinical trials. The special or additional physics tasks that are required both to become credentialed and to meet specific protocol quality assurance and data submission requirements. The quality assurance review process and how is the submitted data evaluated. How QA affects the statistical analysis of clinical trials. The data review and resource centers that receive the data submissions and what they do. And we'll talk a little bit about physics resource requirements. So it's 7:30 in the morning and you're up to your ears in quality assurance in your own department. Why should you care about clinical trial quality assurance? Well, your efforts to ensure that treatments are delivered per protocol guidelines are critical in establishing the statistical significance of the findings of the clinical trial. Radiation therapy trials are using more complex treatments than in the

past, IMRT, stereotactic, radiotherapy and brachytherapy. And the NCI has created a new program which permits and encourages much wider participation in clinical trials throughout the country. In fact, there is a good chance that radiation therapy departments that have not seen protocol patients in the past will begin to see them. And if you've had protocol patients in the past you may see more than before. Your role is that you're expected to be a knowledgeable resource to the radiation oncologist and staff in correctly delivering treatments to protocol patients. You are responsible for all aspects of the quality assurance of clinical trials in which the radiation oncology department participates. That includes credentialing to be a clinical trial center, performing various benchmark tests, reading and understanding each protocol, performing protocol specific QA, creating and submitting the required data to the QA

centers. And if you consider that one protocol can involve hundreds of radiation therapy departments, that there can be INTRA-department treatment variations, there can be INTER-department treatment variations. The radiation therapy guidelines within the protocol are there to minimize variations, to assure that patients from any department are treated comparably. Your role is to ensure that the protocol radiation therapy guidelines are applied correctly. So this reminds me of the biblical story of the Tower of Babel where God cast a thousand languages upon the myriads who were building this tower to the heavens to try to foil their efforts. Babel comes from the Hebrew word for confusion and this is to say that the quality assurance practices and the quality assurance for clinical trials infrastructure in the country is there to reduce

confusion so that we all speak the same language when we're treating patients on clinical trials. And as a matter of fact, in Southern Iraq a number of structures that look something like this were

found. They're called ziggurats and archeologists believe that the Tower of Babel was one of them. So let's talk a little about what is a clinical trial. The National Cancer Institute's cooperative group program, the Cancer Therapy Evaluation Program, and what have we learned from radiation therapy clinical trials. Clinical trials are research studies designed to answer specific questions about the effects of a new therapy or technique designed to improve human health, including developing better methods of treating diseases like cancer. It tests new combinations or methods of treatments to determine are they safe or either superior or at least as effective as existing therapies. And in fact, many of today's standard treatments for cancer began in clinical trials. Statisticians and statistics play an important role in clinical trials. Statisticians define the size of the outcome difference thought to be medically meaningful and they calculate the sample size required to provide some fixed assurance that if a specific difference in

outcome exists the analysis of the study data will lead to a statistically significant result. So for example, if you want to test whether stereotactic radiosurgery prolongs survival compared to whole brain irradiation for patients with brain metastasis, you would hypothesize some increase in survival from the radiosurgery treatment. You would give this to the statistician who will look at what the mean and standard deviation of the survival is for the whole brain irradiation patients, and applying certain accepted criteria for confidence levels will tell you that, for example, you need 250 patients in each arm of the study in order to come up with a statistically significant result. It's very important to note that efforts to reduce the variability in the treatment delivered are likely to increase the power to detect important differences and outcome by treatment. So let's look at what the protocol does in a clinical trial. It explains the reason for doing the study, what are the end points, how many patients will be in the study, who is eligible to participate, what

.study drugs or therapies will be given, what medical tests they'll have and how often, what data will be gathered, what adverse events are anticipated and how they'll be dealt with, and the requirements for patient consent and authorization. Novel radiation treatments must successfully complete three phases of trials before the FDA approves them for general use. In Phase I trials we determine is the new treatment safe. In Phase II trials, is the new treatment effective. And in Phase III trials, is the new treatment better. In 1955 Congress established the NCI's Clinical Trials Cooperative Group Program. Now in the example I gave with radiosurgery versus whole brain irradiation, you are told you need 500 patients in this study. Perhaps in your small department you see 12 of these patients a year. Well, you would retire before you saw enough patients to complete the study. So what you do is you enlist the help of 50 other institutions who each see some number of these patients, and so that in a one or two year

period of time you could complete the study. Currently there are 1500 institutions in the United States that are participating in cooperative group clinical trials treating 20,000 new patients annually with over 1,000 treatment trials, and thousands of investigators. And again, the purpose is to develop and conduct large scaled multi-institutional trials. So the NCI has four major

programs designed to make clinical trials widely available in the United States. NCI comprehensive clinical cancer centers perform clinical trials independently. And then there's the cooperative clinical trials program which, for example, the RTOG is an example. And in organizations like the RTOG, they have perhaps hundreds of member institutions who have all agreed to submit some minimum number of patients each year to participate in the clinical trials that the group runs. In addition, there's the Community Clinical Oncology Program and the Cancer Trial Support Unit. The CCOP makes clinical trials available in a large number of local communities in the

United States by linking community physicians with researchers in cancer centers. CCOP's allowed potential investigators to participate in a majority of cooperative group trials including Phase I, II and III trials. Potential CCOPs must have a proven track record to accrue to NCI sponsored treatment prevention and control trials. The Cancer Trial Support Unit was established by the NCI in 1996. It offers and facilitates individual participation in a selection of NCI sponsored cooperative group Phase III trials to qualifying oncologists who are not members of a cooperative group. It permits institutions that are members of one study group to enroll patients in trials run by another study group. And most interestingly and importantly, it permits institutions that are not members of any study group to enroll patients in clinical trials. To participate in this program you submit an application, you fill out a facility questionnaire, you agree to be monitored by the RPC, you pass the necessary credentialing tests. CTSU members are not

required to demonstrate prior experience in clinical trial participation and have no accrual requirements. It is the activity of the CTSU program that may increase your number of protocol patients, at least that's what the NCI hopes. You may not know that of all the cancer patients that are treated with radiation therapy each year, less than 5% of them are on clinical trials and NCI hopes to increase that number. The Cancer Therapy Evaluation Program is a program within the NCI that works extensively with the pharmaceutical and biotechnology industry to effectively develop new cancer treatments. They formulate the research priorities for the NCI and their protocol review committee reviews all proposed protocols and must approve them before activation. So let's talk now about what have we learned from clinical trials that use radiation therapy. Clinical trials have served to define the standard of care for many diseases. For example, the benefit of chemo radiotherapy in both cervix cancer and rectal cancer and has confirmed

the equivalent local control and survival benefits of mastectomy and lumpectomy with radiation therapy. In the United States today more than 70% of children with cancer live at least five years after diagnosis as opposed to only 55% in the mid 1970s due primarily to the improved treatments validated in cooperative group trials. And much of the data presented in our medical journals are the result from clinical trials. Over the last 30 years improvements in treatment consistency and quality assurance methods have been developed. Differences between planning systems, imaging methods and human interpretation are better understood. And it's important to realize that we have seen that deviations in delivered treatments can result in increased treatment failures. And a few examples of this is a Ewing's protocol by the children's group previously known as the Pediatric Oncology Group now the Children's Oncology Group, found that only 16% of patients have local control of their primary disease when their treatment volumes were

inconsistent with study guidelines compared to 80% for those treated consistent with guidelines. In a German Ewing sarcoma study, 90% of local relapses occurred in patients with radiotherapy protocol deviations. In a German Hodgkin's study, treatment success was 12 percentage points higher without protocol deviations. And we've also learned that centralized pretreatment review has decreased the deviation rate from 30% to 6%. So let's talk about the physicist's role in clinical trials. We'll talk about protocols that involve the physicists cooperative group membership efforts, how do we assure protocol compliance, understanding image-based protocol prescription and target volume specifications, protocol data submission to QA centers, Social measurements and calculations and what have physicists contributed to this process. Any trial using radiation therapy will involve the radiation physicist. The rigorousness of the quality assurance and data submission is related to whether or not the protocol is

testing radiation therapy. There may be special calculations you need to perform. There may be requirements to treat or prescribe dose in an unfamiliar way. ICRU nomenclature may be used and there may be requirements to contour organs at risk and limit their doses to given values. We'll take a momentary artistic interlude here. This is the Tower of Babel by Gustav Doré. Now you may be involved in helping your institution become a cooperative group member, for example, the RTOG, and if that's so then you'll be involved in filling out the application for membership. Your institutional review board must improve your department's involvement, you may be involved with that. Specifically the physicist is responsible for providing documentation on the types of accelerators used for treatment, diagnostic equipment used for definition of tumor volume and simulation, treatment planning systems used for generating the treatment plans for external beam and brachytherapy, the equipment used for any special

procedures like stereotactic radiotherapy, physics and dosimetry equipment used for calibration and quality assurance, institutional QA procedures on all the accelerators and other equipment used for patient treatments, and an independent confirmation of the calibration of your megavoltage beams. Some of the areas which a physicist is expected to participate in assuring compliance with protocols is to complete credentialing benchmarks, ensuring that the treatment plan is consistent with the radiotherapy guidelines for target dose, dose uniformity and the organ at risk dose, providing the special measurements or calculations required, and providing the data output for submission. So let's look at the anatomy of the radiotherapy section of a protocol. You will find these elements includes specification for the treatment machines and modalities allowed for treatment, the target volume, treatment volume and critical normal tissue definitions, treatment planning, imaging and localization requirements, patient

immobilization, dose prescription and specification, treatment verification, radiotherapy toxicity, adjustments and toxicity reporting guidelines, compliance criteria and other information specific to that study. Your job is to read and understand these sections. So let's talk about understanding image-based protocol prescription and target volume specifications. More and more radiotherapy protocols are allowing advanced technology and, for example, 3D conformal IMRT, and these you require ICRU 50 and 62 nomenclature. Also realize that dose prescription criteria, meaning the dose to be delivered, can be different from the dose specification criteria which is the dose to be reported. A couple examples which point up the differences that you can find from one protocol to the next if, for example, in an RTOG lung protocol prescription dose

was the dose at isocenter, the ICRU reference point, with an additional requirement that a minimum of 93% of this reference point dose covered the PTV. In an RTOG prostate

protocol it was worded differently. Prescription dose was 1.8 gray per fraction minimum delivered to the PTV with a maximum point dose no greater than 7% higher than the prescription dose. So it's important to realize that there are these distinctions from one protocol to the next and to read these carefully so that you can comply with whatever the particular protocol is requiring. Also note that the maximum dose specification is moving away from relying on a single point or voxel. Instead, the maximum dose to a small stated percentage of the volume of either the PTV or of all tissue within the body is specified. There are some special measurements that you might be expected to make. We'll talk about a few related to external beam. Treatment delivery system specific dosimetric parameters you might have to measure. For example, for radiosurgery protocols mechanical and radiation beam alignment of the linear accelerator, off-axis radiation beam characteristics including off-axis ratios and beam hardening and

softening might be required for a TBI protocol. Or skin and surface doses. And for TBI protocols validation of the inverse square law of the extended distances used in that treatment may need to be measured and verified. For patient specific measurements you may need to measure and estimate the dose to certain critical structures, like the eyes, lens, the gonads, spinal cord. You might have to estimate the average internal organ motion, for example, in a lung tumor protocol. You may need to measure the transmitted dose through partial transmission blocks. An example there would be for TBI or Hodgkin's protocols. And for TBI protocols the delivered dose rate at the midline of a patient at the extended treatment distance. There are also special calculations you'll encounter. For example, renormalization of dose distributions to comply with the protocol prescription, specific point dose calculations, dose calculations with or without inhomogeneity corrections, dose to organs at risk, and dose volume

histograms for target volumes, OARs and other specified normal tissues. So let's talk a little bit about protocol data submission. Timely and accurate data submission is essential. You may encounter protocols that have pretreatment review which means that you have to submit some preliminary data before the first day's treatment or rapid review in which you need to submit data within the first three days of the treatment. And some advanced technology trials require electronic data submission. So if it's a rapid review situation, the preliminary dosimetry information you would be expected to submit would be the radiation therapy prescription, patient setup data, simulation films, DRRs, portal images, dose distributions and monitor unit calculations. And, for example, isodoses. For all protocols, usually within about a week of completion of the treatment, final dosimetry information is required which would include the daily treatment record, dosimetry data that may be different from the preliminary submission including

dose distributions, calculations, measurements, dose volume histograms, isodoses, and patient setup data for any fields that were not initially submitted. So where does this information go? There are three major national quality assurance review centers and each is unique in its own right. There's the Quality Assurance Review Center, there's the Radiological Physics Center, and the Radiation Therapy and Oncology Group headquarters QA office. Each of these has

agreements with various cooperative groups to provide a range of quality assurance services, including chart, film, procedure and dosimetry review. The RPC has worked with all of the cooperative groups. The Radiation Therapy and Oncology Group QA office does quality assurance for the RTOG only. And then QARC is somewhat unique in that it deals with the diversity of cooperative groups, both adult and the national children's oncology clinical trials group. Now in addition, there are two national resource centers. There's the Image-Guided Therapy QA

Center or the ITC, and the Resource Center for Emerging Technologies or RCET. Their mission is to develop and provide electronic data archival and retrieval services. So as I mentioned, the Quality Assurance Review Center was created in the late 1970s and it provides a wide range of QA services to a host of different adult and children's cooperative groups. The RPC was established in 1968. It monitors some aspects of dosimetry for all of the active NCI funded cooperative groups and several intergroup activities. It has implemented a quality assurance program that monitors the basic machine output and brachytherapy source strengths, the dosimetry data utilized by your institution, the calculation algorithms used during treatment planning, and the institution's quality assurance procedures. You may be familiar with the mailed TLD program that they had going for a number of years which is to verify your output calibration. They also have mailed anthropomorphic phantoms to verify tumor dose delivery for special

treatment techniques. In this graph we see that currently 5,000 TLD blocks are irradiated for photons and electrons, and in fact the mailed TLD programs presently monitor more than 90% of the estimated 1650 radiotherapy facilities in the United States. The RPC routinely monitors all conventional therapies, including external beam megavoltage photon and electron beams as well as brachytherapy. It may be interesting for you to note that if your TLD dose discrepancy exceeds 5% that you may become a candidate for an immediate visit by the RPC. When the RPC physicist comes to your institution in such a case, they attempt to identify the origin of the discrepancies at the 1% level if possible, 5% discrepancies of tumor dose are pursued aggressively. So here are the four RPC anthropomorphic phantoms. There's the stereotactic, the IMRT head and neck phantom, the pelvic phantom, and the thorax phantom. So you receive these in the mail. There's a dosimetry insert for each which includes TLDs and radiochromic film.

This goes inside the phantom, you fill the phantom with water, you CT it, you treatment plan it, you radiate it, empty the water and ship this back to the RPC along with your dosimetry information on what dose you think you gave. The RPC evaluates the dosimeters inside and compares your stated dose with their measured dose. The RTOG QA center is affiliated with the RTOG, of course, and the American College of Radiology. Their job is to assure compliance with protocols in all aspects of radiation therapy, dose prescription and delivery. They have a medical dosimetrist's QA review for advanced technology clinical trials. They do patient registration and clinical outcome data management and statistical support for ongoing RTOG trials using advanced technologies. They design, monitor and do analysis for new clinical trials using advanced technologies. And they maintain and improve the current electronic link between the RTOG's clinical trial database and the ITC's treatment planning and verification database. The Image-

Guided Therapy Center, the first of the two national resource centers, was started in 1992, was created to provide quality assurance for multi-institutional 3D conformal radiotherapy trials sponsored by the RTOG. It approves participants in the 3D CRT trials by ensuring that they meet the minimum technical requirements for participation in these protocols and they understand the protocol requirements. They facilitate quality assurance reviews by the QA review centers and they develop a database to accommodate all of the treatment planning verification and clinical data submitted to the ITC. The second center, the Resource Center for Emerging Technologies is at the University of Florida, was established in April of 1999 to develop and disseminate resources that would facilitate the conduct of NCI sponsored advanced technology clinical trials. They have developed an infrastructure for distributed database, visualization and analysis systems for collecting, sharing, distributing information generated by the

multitude of institutions participating in clinical trials, and importantly they facilitate remote review of protocol data. In 2002 the NCI awarded a five-year grant provided that the five centers, the three quality assurance review centers and the two national resource centers, join to become the Advanced Technology Consortium, or ATC, to coordinate efforts, reduce duplication and unify the quality assurance practices across the country. The mission of the ATC is to develop and provide credentialing of institutions to participate in advanced technology trials, to develop basic technical and QA criteria for each protocol assessed, provide a mechanism for both prospective and retrospective review of image-based treatment plans to assure that they are within protocol specifications, and to develop and maintain a comprehensive database of treatment planning and verification digital data including tumor and normal structure contours and 3D dose data which can be correlated with treatment outcomes. Please plan to

attend the ATC symposium this Wednesday at 4 PM in Room 303. So let's look at this hierarchy of the clinical trials quality assurance infrastructure within the country. The National Cancer Institute funds and facilitates the existence of these various organizations. In yellow are the various cooperative groups. QARC, RPC and the RTOG are the quality assurance review centers. RCET and ITC are the two national resource centers. Collectively these five are the ATC. The arrows indicate the participation and cooperation from one group to the next. So for example, the RPC does dosimetry and quality assurance for all the cooperative groups. QARC deals with these..the RTOG QA center deals with the RTOG. And all three of these quality assurance .review centers depend on these resource centers because they archive the digital data that's being submitted so that the review centers can then have that data reviewed. And this is a picture of the Tower of Babel by 16th century artist Pieter Bruegel. Now there are

two schemes for getting data from your treatment planning system to a national resource center like the ATC. The existing system is referred to as FTP or media base transfer. And the way this works is that your treatment planning system, most treatment planning systems, can export RTOG data, some can export DICOM RT data. You can FTP this information to the ITC file server or you can make a CD or a tape and mail that to them, in which case that will be manually manipulated and reorganized and will go onto a web server so that reviewers can remotely review this data. This is a very important new feature of the clinical trials quality assurance infrastructure in this country is to permit remote review so that instead of having some number of

principal investigators and study chairs having to fly to the offices of the QA review center and sit there for days looking over films and hard copies of isodoses, at their office on their own time they can get onto the computer and through the web they can review the data that they are

supposed to review. And in fact, if data is submitted via DICOM RT including 3D dose grids, they could potentially redraw a target volume that they disagree with, recompute the dose volume histogram and then determine if the corrected target volume complies with the protocol guidelines. Another important feature of this initiative is that in the future if there are patients who fail treatment, one could go back to the 3D dose grid that's also available with the CT anatomy data and try to correlate the recurrence of the failure site with the dose at that site or for toxicities to try to go back to make a correlation between the dose and the severity of the toxicity. The new scheme which is still under development will eventually work in the following way that your system, your treatment planning system, will export data via DICOM RT through the web directly to a ATC server called the WebSys server and that data will immediately become available for remote review. Currently there's still some manipulation that has to go

on to organize the data and parse it out in the right places, but eventually that would be the vision. Now all of these efforts have had a great deal of participation by medical physicists. I wanted to just recognize that. Medical physicists have been instrumental in the development and review of protocols. The RTOG and COG have physics subcommittees. Within the quality assurance review and resource centers, medical physicists play a key role providing advice on and reviewing protocol language, doing case reviews of submitted dosimetry, helping to design special quality assurance tools and doing radiotherapy department inspections. Now consider the QA problem that we're trying to deal with. Consider that hundreds of radiotherapy departments may be treating patients on a given protocol, each with different treatment planning systems, treatment machines, perhaps different calibration protocols, different dose prescription practices, but we want all these patients to get the same dose. Let's talk about the quality

assurance review process a little bit more now. We'll also talk about benchmarking and credentialing and how are the data that are submitted actually evaluated. There are some multiple levels of quality assurance review, for standard radiotherapy where radiation is not the study question. For example, for an ALL protocol where a full brain irradiation is given to all the patients and the study is testing chemotherapy agents. Perhaps chart review would be done to determine the correct dose and fraction size. If the radiotherapy is not the study question but toxicity and efficacy of radiotherapy is of interest, for example in a lung cancer protocol where again the same radiotherapy is given to all the patients and the study is testing different chemotherapy agents. However, here a review of target volumes, treatment plan, dose to specific organs and port films would be conducted. And where radiotherapy is the study question, a more comprehensive review would typically be done. For example, the children's oncology

group has a new trial for medullo blastoma in which they're testing reducing the dose and the volume irradiated, requiring 3D conformal radiotherapy and allowing IMRT treatments. Here treatment plans including target volumes and fields would be reviewed within three days of the start of the treatment. Doses would be checked along with QARC films compared to DRRs and, in fact, changes to the plan could be suggested by the QA center. There are a host of benchmarking and credentialing tasks that you may faced with. QARC has a set of what's called

standard benchmarks. It includes running a treatment plan on wedged fields, irregularly shaped fields, central axis blocked field, and craniospinal irradiation. There is a 3D treatment planning benchmark. There's a 3D CRT facility questionnaire. There's an IMRT questionnaire and benchmark which may also include an anthropomorphic phantom irradiation. There's a total body irradiation benchmark, and a stereotactic radiosurgery benchmark including an

anthropomorphic phantom irradiation it can be used with either gamma knife or linear accelerator. And there's prostate brachytherapy credentialing. Some of these require dry run electronic data submission. Now this is an example of the QARC irregular field benchmark where you're given a typical drawing of an irregular field, position of the central axis, a point B and a point C, the depths to these points, the SSDs, and you're asked to calculate the monitor units to deliver 90 centigray at the midplane on the central axis and then to calculate what dose point B and point C would get. This is the ATC IMRT benchmark. This particular benchmark has been in the literature recently. The PTV is in white. The organ at risk here is in green with these dimensions as shown. The aim of this plan is to deliver the prescribed dose of 200 centigray per fraction to 100% of the PTV and not more than 120 centigray or 60% of the prescribed dose to more than 5% of the organ at risk. And that no point within the irradiated volume should get more than

120% of the prescribed dose. Data submission in this case includes planning dosimetry and verification dosimetry so that you actually irradiate a phantom with film and ionization chamber and submit those results. So how is the data that you spent all this time submitting actually get evaluated by the review center? Treatment is scored by the QA center and/or the principal investigator as either compliant or minor violation or a major violation or unevaluable. This depends on the adherence to the protocol criteria and completeness of data submission and patient eligibility. Volume and dose are scored separately. So for example, this is the deviation definitions from a particular protocol. For prescription dose, a minor deviation is stated as the dose to the prescription point differs from that in the protocol between 5 and 10%. And for a major violation the dose to the prescription point differs from that in the protocol by more than 10%. For dose uniformity there's a separate statement. Minor deviation if the

variation of the dose in the target volume exceeds +7 or -5%, but is within plus or minus 10%. A major deviation would be the variation of dose in the target volume exceeds +14 or -10%. And then separately for volume a minor deviation would be that the margins of the fields are less than specified or excessively large. A major volume deviation would be that your fields are transecting tumor or potentially tumor bearing areas. It's interesting for you to understand that the outcome of all patients who are eligible to be on a study are included in the final statistics for outcome no matter what their violation status is, even if they were on a radiotherapy arm and didn't get any radiation. This is the principle of intent to treat. And the logic of that is that if there is a protocol to treat a certain disease with radiation therapy and some number of patients are non-compliant, they're assigned to a radiotherapy arm but are non-compliant and don't get radiotherapy, or they start radiotherapy and get too sick to finish, or for some other reason don't

get the dose they're supposed to get, that that's a feature of the disease and the treatment plan. And that if you in the community were going to get 100 patients of this type for this treatment that you, too, would expect to get some number of patients who couldn't complete the radiation

therapy. So to be the most conservative in stating local control and survival statistics, you need to include those patients. That's the logic of this intent to treat. However, subset analysis is frequently done to try to tease out whether the patients who actually got the prescribed protocol dose without major violation did better than those who didn't. So what happens to this scoring data? The final scores for these patients is recorded and sent to the operations and statistical offices of the cooperative groups and to the PI and RT PI of the institution that treated the patients. So they're keeping score. The compliance scores for each institution are sent to the RT QA committee of the group. The composite score of all the patients from each institution

determine the institution's overall performance score. And this performance score is critical in the institution's ability to maintain their participation in the cooperative group. Well, all of these efforts take time and I want to be sure to mention to you what kind of time and resource requirements you might be expected to incur if you were to start participating in clinical trials in your department. There's startup time, cooperative group membership, credentialing, there's routine QA physics support and protocol specific QA support. So for example, for filling out forms for institutional application, this could take you three hours. Doing the standard or 3D benchmark could take four hours each. Doing an IMRT benchmark could take up to a day. And validation of your data exchange software could take hours. Routine and patient-specific QA physics support, the RPC TLD dosimetry program could potentially take you one to two hours. Time to fill out data submissions forms for a protocol that uses standard

radiotherapy, maybe 30 minutes. For a more complex protocol using 3D or IMRT, you need to generate DRRs, DVHs, specific isodoses and associated forms, this could take two hours each. And submitting these data once created, another half hour or so. In summary, in the near future facilities and the physicists which have not had a significant exposure to clinical trials involving radiation therapy will encounter an increasing number of patients on national clinical trials due to the CTSU program. The clinical radiation therapy physicist has a large and important role in the success of clinical trials involving radiation therapy by ensuring that the patients at his or her facility are treated per the protocol specifications, that the treatment equipment is quality assured and that the treatment plan data and other required dosimetric data are submitted accurately and on time to the Quality Assurance Review Center, realize that a significant amount of physics time may be required in this effort, and that physicists must be

aware and able to provide the services necessary to comply with advanced technology protocols. Please watch for the release of the AAPM report number 86, Quality Assurance in Clinical Trials: A Primer for Physicists. This should be coming out in the next couple months. Thank you very much and I'd be happy to take any questions you have.