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Stereotactic Irradiation for Intracranial Tumors

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Radiation has been used for the treatment for different types of intracranial lesions for many years. It has been used in the treatment of benign tumors such as meningioma, vestibular schwannoma (also known as acoustic neuroma), and craniopharyngioma. Radiation has also been used in the treatment of malignant brain tumors such as astrocytoma, medulloblastoma, or brain metastasis. Radiation has also been used in the treatment of arteriovenous malformation and trigeminal neuralgia.

There are different types of radiation treatment modalities. They in general can be grouped into three categories - conventional radiation therapy, fractionated stereotactic radiotherapy, and stereotactic radiosurgery. Stereotactic radiosurgery is the delivery of stereotactic radiation in one single fraction. The prototypes of stereotactic radiosurgery are Gamma knife, LINAC, proton, and Cyberknife. Fractionated stereotactic radiotherapy is the delivery of highly focal stereotactic radiation in a fractionated schedule (multiple fractions). Fractionated stereotactic radiotherapy combines the precision of stereotactic positioning with the radiobiological advantage of fractionation. In contrast to surgery and radiosurgery, fractionated stereotactic radiotherapy treatment is non-invasive. The prototypes of fractionated stereotactic radiotherapy are LINAC, proton, and Cyberknife.

This slide demonstrates the typical isodose of conventional radiation therapy using opposed lateral radiation fields. This is a contour of a patient with brain tumor. These are the eyes. These are the optic nerves. This is the brain tumor. This is the brainstem. In conventional radiation therapy, we usually deliver radiation from the left and the right. Usually CAT scan and MRI are not required as part of the radiation planning. The numbers shown on this slide represent radiation dose lines. For a good radiation plan, we want 100% to cover the target, and we want the dose delivered to the non-target normal tissues to be as low as possible. As you can see here, with the use of opposed lateral radiation fields delivered by conventional radiation technique, the dose coverage to the tumor is 100%. However, the dose to the normal tissues such as the brainstem is as high as 122%. We don't usually use this type of radiation for most brain tumors except in patients that require whole brain radiation, such as patients with breast or lung cancers with brain metastases.

What are the side effects of brain radiation using conventional radiation technique? During radiation, patients can experience fatigue, hair loss, skin irritation, and nausea or vomiting. After radiation, patients can experience hormonal dysfunction, bone deformities, hearing loss, memory loss, cognitive dysfunction, or radiation-induced cancer. Obviously, for most patients with brain tumors, we need something better than the conventional radiation therapy.

This brings us to stereotactic irradiation. What is stereotactic irradiation? Stereotactic irradiation is the delivery of stereotactically guided and highly precise radiation that is used to inactivate tumor growth. There are two main types of stereotactic irradiation. The first one is stereotactic radiosurgery, which is stereotactic radiation that is given in one single treatment. The second type is fractionated stereotactic radiotherapy which is the stereotactic radiation that is given in multiple treatment sessions, usually during a five to six week-course of daily radiation treatment.

What are the basic principles of stereotactic irradiation? Instead of using two radiation fields as in conventional radiation technique, multiple non-coplanar intersecting radiation beams from different angles are commonly used in stereotactic irradiation, as shown in this picture. By using stereotactic irradiation, all the radiation beams are converged in the tumor and the normal tissues receive a very low dose of radiation. Stereotactic irradiation is a very precise form of radiation; patients require a special immobilization device to immobilize the head while undergoing radiation treatment. This slide depicts the dose comparison between conventional radiation and stereotactic irradiation. With the use of stereotactic irradiation, the dose received by the normal tissues is decreased from 122% to 5% in this case.

What are the different types of stereotactic delivery systems? In general, there are four types of stereotactic irradiation techniques - they are protons, Gamma knife, stereotactic linear accelerator, and Cyberknife. This is a Gamma knife machine. It uses 201 Cobalt sources. There are approximately 35 Gamma Knife centers across the country. Gamma Knife is particularly good for treating small lesions. The disadvantage is that it can only perform radiosurgery; it cannot perform fractionated radiation. For patients that receive Gamma Knife radiosurgery, their heads have to be immobilized by external head frames that are attached to their skulls by screws.

This is CyberKnife. CyberKnife consists of a robotic arm that can freely move around a patient. It has also an X-ray tracking device that can track patient's movement during radiation. CyberKnife can perform both single dose and fractionated irradiation treatments. Patients do not need invasive head frames.

This is a linear accelerator or LINAC. This is the type of radiation machine that is most commonly used - the same machine that is used to treat breast cancers, lung cancers, prostate cancers, etc. For patients with brain tumors, specialized equipments are attached to the LINAC. This machine can be used for single dose or fractionated stereotactic irradiation treatments. For single dose radiosurgery, patients need invasive stereotactic head frame. For fractionated stereotactic radiation treatment, no invasive head frame is necessary.

This is our proton beam machine at the Massachusetts General Hospital. Proton beam is a very different form of radiation. In contrast to Gamma Knife, CyberKnife, or LINAC, proton

beam is a heavy charged particle. Because it is a charged particle, it has superior physical dose distribution. The dose received by the normal tissues is the lowest compared to Cyberknife, Gamma Knife, or LINAC. The proton machine can be used for single dose and fractionated stereotactic treatments. Proton treatment is currently only available in two places in the United States; they are the Massachusetts General Hospital in Massachusetts and Loma Linda University Medical Center in California.

This is a dose comparison. The green is the tumor target. The red is the irradiated volume - the area of the normal tissue that received a significant dose of radiation. For an ideal radiation plan, one would want radiation to be confined to the green and to have as little red as possible. In order to achieve dose conformality in LINAC or Gamma Knife radiation plans, the targets have to be plugged with spheres of radiation. By doing so, one can actually generate a plan with many radiation hot spots as the radiation spheres overlap with each other. If normal tissues are present within the radiation hot spots, treatment-related complications can be expected. For proton treatment, hot spots are generally not a concern. The proton radiation plans are typically very conformal and homogenous due to the distinctive physical properties of protons.

This slide depicts the dose comparison between proton beam and LINAC radiation. This is a patient with vestibular schwannoma (also known as acoustic neuroma). With the use of proton, normal brain tissue tissues do not get much dose, whereas in LINAC radiation plans, the normal tissues receive 30 to 50% of the prescribed dose.

In summary, there are advantages and disadvantage of different types of stereotactic radiation techniques. For proton, the normal tissues always receive less radiation. It's highly conformal. Proton, however, is currently only available in two places in the United States. LINAC is available across the country. It allows for both single dose and fractionated stereotactic radiation treatments. Its accuracy for small targets is questionable. Gamma Knife is highly conformal for small lesions; it however cannot treat large lesions. Gamma Knife is not made for fractionated treatments. One of the advantages of Cyberknife is its ability to track the target location during radiation. Cyberknife, however, is the latest technique and has less clinical experience.

So which stereotactic irradiation is the best for you? The choice of type of stereotactic irradiation technique depends on the type of the lesion, the location of the lesion, the size of the lesion, and many other factors. Potential patients should be seen by a team of physicians consist of neurosurgeons and radiation oncologists. The next question is when is fractionation stereotactic radiotherapy indicated? When is stereotactic radiosurgery indicated? Fractionated radiation has the longest clinical experience. There is radiobiological advantage of using fractionation.

At the Massachusetts General Hospital, fractionated radiotherapy is indicated when the lesions are large and when the lesions are very close to critical structures, such as the optic chiasm, the optic nerve, brainstem, or cranial nerve. We use fractionated radiotherapy when we want to preserve cranial nerve function, such as hearing, facial nerve, or trigeminal function.

At the Massachusetts General Hospital, proton beam radiosurgery is indicated patients with acoustic neuromas that do not have any functional hearing, when lesions are very small, and for patients without any cranial nerve deficits. We recommend fractionated stereotactic radiotherapy for patients with functional hearing, for patients with pre-existing cranial nerve deficits, and for NF2 patients

In our experience, the tumor control rate of acoustic neuroma was 98% with the use of stereotactic radiotherapy. The rate of preservation of normal facial and trigeminal nerve was 99% and 96%, respectively. Most patients in our study did not have NF2. Eighty-four percent of our patients retained subjective functional hearing after stereotactic radiotherapy.

We have also been using proton beam therapy for the treatment of benign meningioma. The local control rate was 100%. Which stereotactic technique is best for you? My recommendation is go to facilities that have many years of experience and with multiple stereotactic techniques available.

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Does anyone have any question?

Audience Member: Can I ask a question about proton beam at Massachusetts? How many treatment rooms have you got operating there?

Dr. Chan: We have recently opened our second treatment room. At present, we treat about 20 to 30 patients per day.

Audience Member: Because you have to have one treatment room that treats eyes, is that right?

Dr. Chan: Altogether, we have three treatment rooms. One is being used exclusively for eye treatments.

Audience Member: What is the difference? Is it a different system?

Dr. Chan: Different energy and different gantry.

Audience Member: Okay. And what has been the experience with proton for NF2 tumors. Do you have any information on that?

Dr. Chan: We have been using mainly stereotactic radiotherapy to treat NF2-tumors. As more treatment slots are available, we will be able to use proton.

Audience Member: You do fractionated radiation with proton as well?

Dr. Chan: Yes.

Audience Member: Because it would be good.

Dr. Chan: Yes.

Audience Member: So will you be doing IMPT?

Dr. Chan: Yes. Our physics group has been working on the IMPT program (intensity-modulated proton therapy). We will be able to use IMPT to treat patients in the very near future.

Audience Member: 5 years?

Dr. Chan: Yes, approximately.

Audience Member: That's what I'm gathering.

Audience Member: What's IMPT?

Audience Member: They're not available yet.

Dr. Chan: Intensive modulated proton therapy. It will the best radiation treatment as it allows the lowest dose to be received by normal tissues when compared to other types of radiation. We have IMRT (intensity-modulated radiation therapy) at our institution.

Audience Member: Five years away?

Dr. Chan: Yes, approximately. Currently, we have the software to do IMRT plans. In order to apply in clinically, a lot of additional work, including quality assurance, is required.

Audience Member: That's not clear in the literature whether or not you're actually doing it now or whether it's something you're working on.

Dr. Chan: We're definitely working on it. Our group has published dose comparison studies with IMPT.

Audience Member: Active scanning, those things you're working on?

Dr. Chan: Yes.

Audience Member: Thank you.

Audience Member: Can proton beam... I'm not asking you if you're using it, but can it be used on regrowths of acoustic neuroma if you've had prior surgery and if you have prior facial problems? Can it be used on regrowth?

Dr. Chan: If the tumor recurs after surgery, patients can undergo re-resection or radiation such as proton, stereotactic radiotherapy, CyberKnife, etc. If the patient failed previous radiation, they should not undergo radiation again in most cases.

Audience Member: Patient's never had it.

Dr. Chan: Yes, the patient is a candidate for proton or for any type of radiation.

Audience Member: You said if a patient failed radiation they could not get radiation again. I've rarely heard that before. I was fried at that statement.

Dr. Chan: The best would be to undergo surgery if a patient failed radiation, in most cases. There is always a higher risk of radiation-induced complication for someone receiving radiation the second time, as the normal tissues surrounding the tumor will receive radiation twice. If there are better options such as surgery, we generally do not recommend re-irradiation.

Audience Member: Your statistics show a sample of 9.

Dr. Chan: Yes.

Audience Member: But I know that they treated more nf2 patients at Mass. General.

Dr. Chan: Between 1992 and 2001, we have only treated nine NF2 patients with the stereotactic radiotherapy technique.

Audience Member: I know your colleague, and he gave me a number of 50.

Dr. Chan: 50 NF2 patients?

Audience Member: 50 NF2 patients.

Dr. Chan: No. We have treated 71 patients with stereotactic radiotherapy between 1992 and 2001. Among them, 9 have NF2.

Audience Member: With a sample of 9, is that convincing evidence?

Dr. Chan: It is not convincing evidence. That's why I emphasized the small number of NF2 patients. Our study will come out soon.

Audience Member: I'll be the devil's advocate here. You said that with Gamma knife you can't fractionate it, yet we have a doctor and I know he does fractionated Gamma knife.

Dr. Chan: Gamma Knife is not designed to do fractionated radiation treatment. For a patient to undergo fractionated Gamma Knife treatment, his or her head has to be screwed to a stereotactic frame repeatedly before each treatment. Non-invasive stereotactic frames are used for fractionated radiation treatment by LINAC, CyberKnife, and proton.

Audience Member: The doctor who does the Gamma knife fractionated, he keeps the person in the position for six days in a row and that's how he does it, and he does it four times and five times.

Dr. Chan: So, patients will have the stereotactic frames screwed to the heads repeatedly or the frames have to be remained attached to their heads for a prolonged period of time.

Audience Member: Yes. Like 5 days, 6 days.

Dr. Chan: In my opinion, the greatest advantage of fractionation is when you do a pure fractionation schedule - once-daily radiation 5 days a week for a consecutive of 6 weeks. When fractionation radiation is only performed 5 or 6 times once a week or so, we call it hypofractionation. The clinical experience of hypofractionation is very limited.

Audience Member: I understand that there's proton in Texas and Florida. Will you open up a(nother) proton beam in Mass. General?

Dr. Chan: University of Florida in Jacksonville, MD Anderson in Houston, University of Pennsylvania, and Indiana University in Bloomington will soon be able to treat patients with proton. At present, there is no plan to open another proton facility in Massachusetts.

Audience Member: Can I ask, the graph on benign meningiomas, it must have had some nf2 patients in there?

Dr. Chan: Actually, no. That was a randomized trial. In that trial, none of the patients had NF2.

Audience Member: Okay.

Paul: It was specifically screened out?

Dr. Chan: No, NF2 patients were not excluded from the study.

Paul: Since that's so common in nf2 patients, is it possible, I think that's what Rose Marie was asking, that you had an nf2 patient?

Dr. Chan: Meningioma is the second most common tumor in NF2 patients. But overall, meningioma is a lot more common in non-NF2 patients than NF2 patients.

Audience Member: There was a speaker a year or two ago from England who suggested that radiation therapy to acoustic neuromas can or has caused malignant regeneration. What is your experience with that and how common is it?

Dr. Chan: Yes, radiation to any site of the body can potentially induce cancer or cause malignant transformation. Radiation in the form of Gamma Knife has been shown to cause malignant transformation of acoustic neuroma. This has been published. Overall, the risk of radiation-induced cancer is very small. But this is something that we have to keep in mind as radiation-induced cancer is usually very aggressive and not curable. In order to minimize the risk of radiation-induced cancer, one has to minimize the amount of normal tissue receiving radiation and the dose to the normal tissue. This is one of the main reasons why we advocate proton, especially in children. We have been using proton and fractionated stereotactic radiotherapy for more than 10 years; we have not seen any radiation-induced second cancer. Radiation-induced cancers can occur many years after radiation. We have to continue to follow our patients.

Paul: I have a question. A post treatment complication is swelling, and it is typically treated with steroids, steroid therapy. It's been documented that nf2 people are especially hyper sensitive to steroid therapy and there is some history of severe complications from the actual steroid therapy. Are you following up on that in your studies?

Dr. Chan: Steroid therapy, especially when used long term, can cause side effects in any patients. I am not aware NF2 patients are more sensitive to steroids. But in general, NF2 patients have larger tumors than non-NF2 patients, and they tend to have higher risk of treatment-related complications.

Audience Member: I think sometimes there's more than a machine involved in the success of the treatment.

Dr. Chan: Exactly. The success of a treatment depends on the size and type of tumor, patient's medical condition, technique and machine availability, and the experience of the physicians and institution.

Audience Member: Can you walk us through, who are all the other people besides the machine? Which people are involved in making the decision?

Dr. Chan: It depends on where you go. If you go to some surgery-oriented facilities, surgeons will make most of the decisions. If you go to the Massachusetts General Hospital, the decision will be made by a team of physicians that consists of radiation oncologists, neurosurgeons, and ENT surgeons.

Audience Member: Because I'm aware of cases where the dosage was really maybe not appropriate and then...

Dr. Chan: Yes. Across the country, people have been using different radiation doses. This is a very controversial issue. There is no general agreement. I suggest patients seek consultations in institutions that have treated a lot of tumors and have published their experience.

Audience Member: Somebody had NF2 and they were thinking about... And they needed some kind of treatment, where would you suggest they go that had the most experience and could lead them down the right path?

Dr. Chan: Depends on what treatment they want, surgery or radiation.

Audience Member: What treatment do you suggest?

Dr. Chan: Whether NF2 patients need surgery or radiation depends on many factors such as 1) age, 2) size, location, and type of tumor, 3) hearing status, 4) neurological function, etc. Patients should have consultations with physicians in multidisciplines.

Audience Member: If they wanted multifractional therapy, where would they go?

Dr. Chan: Massachusetts General Hospital has one of the largest experiences in the United States in the use of conventionally fractionated stereotactic radiotherapy for the treatment of acoustic neuroma. Our experience will be published in the Neurosurgery journal very soon. Across the world, Japan has the largest published experience in the use of this technique.

Audience Member: Proton therapy if they qualify for it, where would they go?

Dr. Chan: At present, patients can go to the Massachusetts General Hospital or Loma Linda Medical Center.

Audience Member: You didn't mention intensive modulated radiation therapy (IMRT).

Dr. Chan: We also have IMRT. For patients with acoustic neuromas, we have been using proton or stereotactic radiotherapy. We have not been using IMRT to treat brain tumors, as other available techniques are very adequate.

Audience Member: I'm not sure what all this verbiage means, but I had a brain tumor in 1984 but I did not become deaf until three years ago.

Dr. Chan: What kind of brain tumor did you have?

Audience Member: I was treated by a laser. I had – I had brain surgery, it was a medulloblastoma. They pulverized it with a laser. Does that relate to Gamma?

Dr. Chan: Laser has not been used for treatment of brain tumors. You probably had some forms of intraoperative radiation. Gamma Knife, proton, stereotactic radiation therapy are all forms of external beam radiation therapy. Sometimes we will give intraoperative radiation therapy – that is radiation is directly delivered to tumors during surgery. Radiation-induced hearing loss increases with time.

Audience Member: What is the size limit you could treat an acoustic neuroma with a proton beam? Is there a size limit?

Dr. Chan: There's no size limit for fractionated proton. There's only size limit for radiosurgery including Gamma knife and proton radiosurgery. When the size of a tumor increases, the dose received by the normal brain tissues also increases proportionally. Patients with large tumors should undergo fractionated radiation treatment.

Audience Member: For five-year old children, we think very small tumors. If the decision is for proton and you say there is a waiting list, how long is the waiting list? How long does one wait to get on this list when we're talking about a five-year-old child?

Dr. Chan: If radiation is indicated in a five-year old child, we will not let him or her wait for long. We always give priority to children.

Audience Member: The options for treatment of acoustic neuroma are either surgery or radiation. Do you have any idea what the relative percentage is across the country, what percentage of patients gets surgery rather than radiation?

Dr. Chan: Ten years ago, more patients received surgery than radiation. Nowadays, more and more patients undergo radiation treatment.

Audience Member: That would only be the patients that are in the areas where that's available, right? Patients in some other part of the country where they're not near these facilities can't get it.

Dr. Chan: LINAC-based treatment and Gamma Knife are available in many places across the country. At present, proton therapy is only available in two places in the US.

Thank you. Very interesting audience. Very good questions.

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