

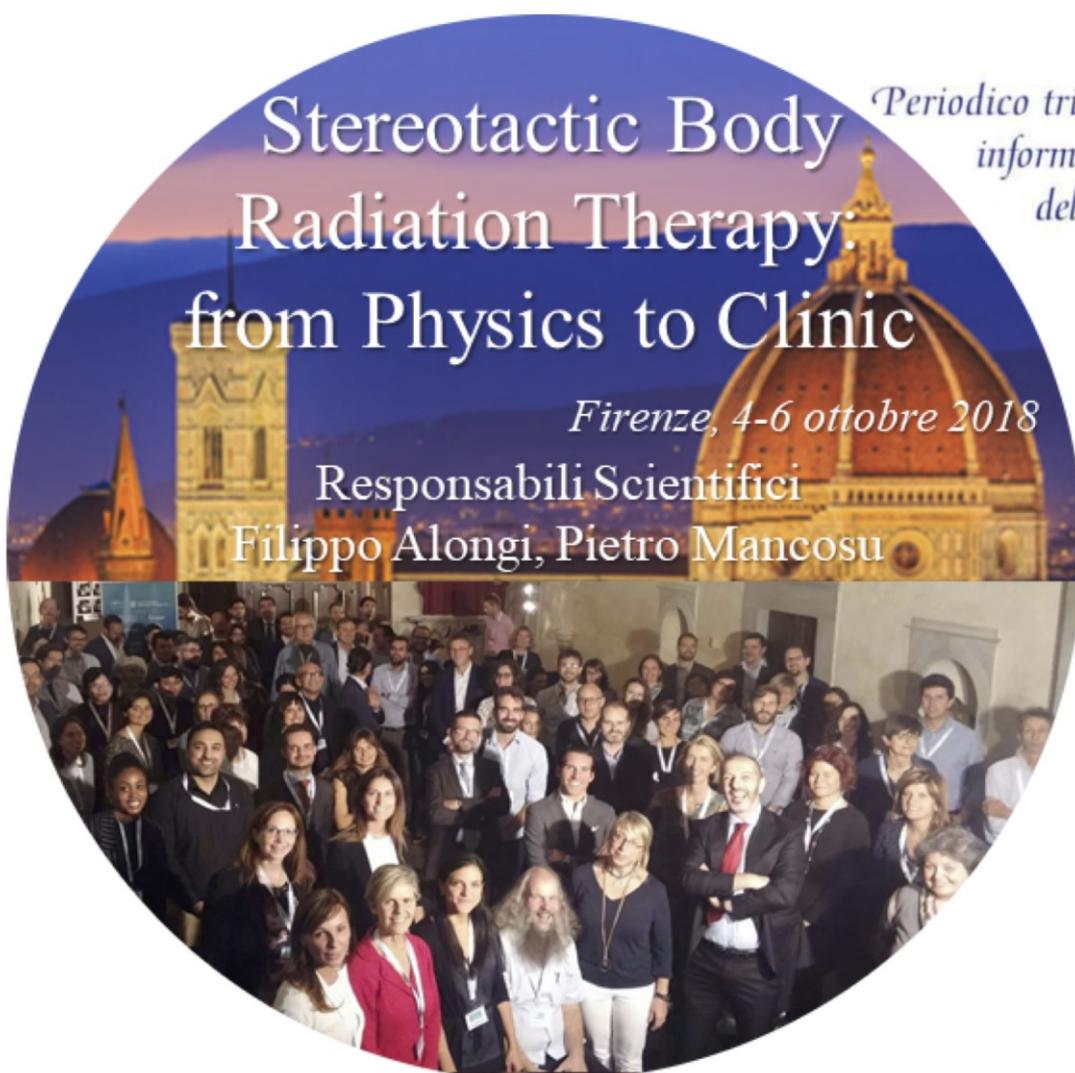
Fisica in Medicina

Stereotactic Body
Radiation Therapy
from Physics to Clinic

*Periodico trimestrale di formazione,
informazione e aggiornamento
dell' Associazione Italiana
di Fisica Medica*

Firenze, 4-6 ottobre 2018

Responsabili Scientifici
Filippo Alongi, Pietro Mancosu



*Numero I - 2019
Monografico*



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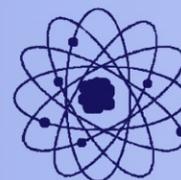
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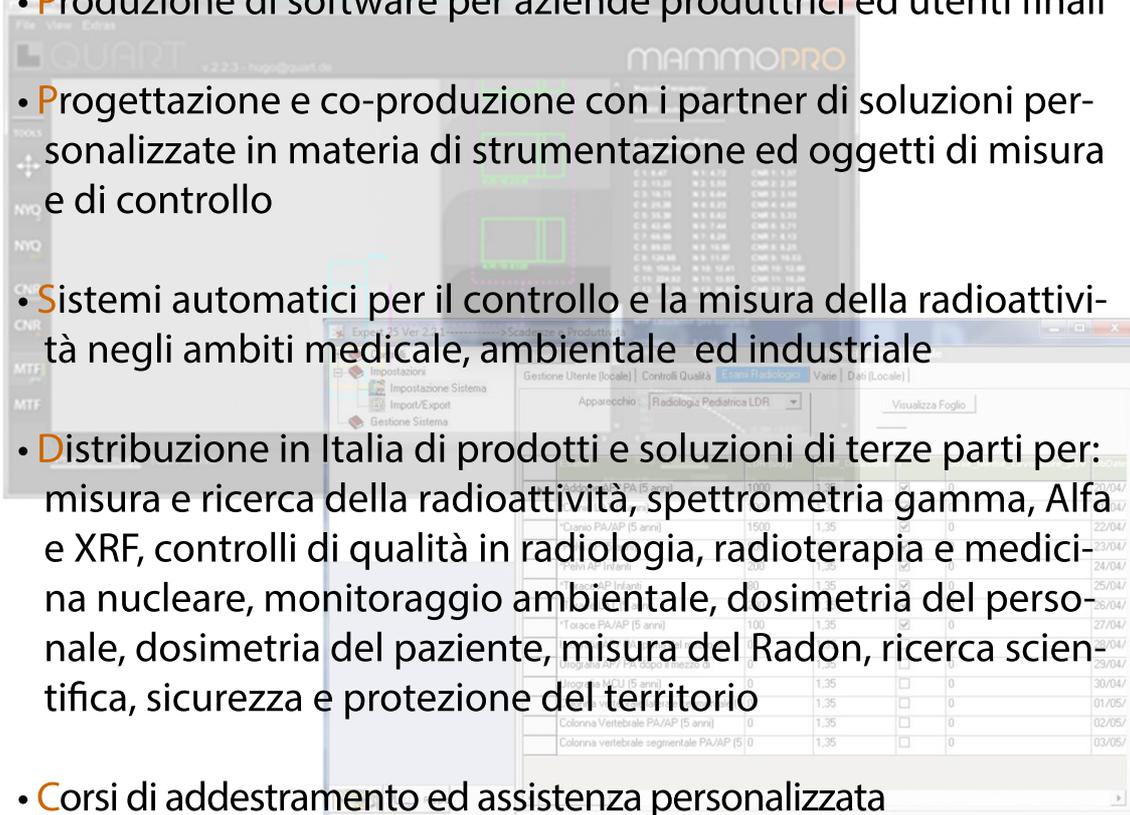
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Introduzione

Questo numero della nostra rivista è dedicato agli atti del convegno internazionale organizzato da AIFM insieme alla associazione Italiana di Radioterapia Oncologica (AIRO) dal titolo "STEREOTACTIC BODY RADIATION THERAPY: FROM PHYSICS TO CLINIC" svoltosi gli scorsi 4-6 Novembre 2018 a Firenze. Il corso nasce in continuità con le prime due edizioni dell'evento svoltasi nel 2014 presso l'aula magna della Università degli studi di Milano e nel 2016 presso l'Università La Sapienza di Roma.

"Modern radiotherapy is increasingly evolving towards a reduction in the number of fractions. Stereotactic Body Radiotherapy (SBRT), or as more recently defined, SABR (Stereotactic Ablative Body Radiotherapy), is a radiation therapy approach in which high radiation doses are delivered in few fractions focused on small extracranial tumors with rapid dose fall off outside the target. In particular, SBRT/SABR is becoming elective therapy, in several anatomic districts, both for primitive tumors and for metastatic lesions. These results were achieved thanks to a multidisciplinary effort with strong involvement of highly qualified and skilled professionals together with technological progress both in imaging and in treatment delivery. Since we consider this multidisciplinary approach as the key of success, the Italian Association of Radiation Oncology (AIRO) and the Italian Association of Medical Physics (AIFM) organize the 3rd edition of the joint symposium on SBRT within the Fuligno monastery area in Florence. "

Con questi obiettivi il comitato scientifico presieduto dal prof. Filippo Alongi e dr. Pietro Mancosu, e composto da dr. Paolo Basitani, dr. Pierluigi Bonomo, prof.ssa Barbara Jerezek, dr.ssa Francesca Romana Giglioli, prof.ssa Stefania Pallotta, e dr.ssa Serenella Russo, ha invitato alcuni tra i migliori specialisti del campo a confrontarsi sullo stato dell'arte della SBRT moderna.

Il convegno ha richiamato più di 240 colleghi fisici medici e oncologi radioterapisti da tutto il mondo. Segno della vitalità e interesse sull'argomento sono stati i 40 e più abstract di carattere fisico e clinico selezionati da un comitato di esperti (prof. Renzo Corvò, prof. Lorenzo Livi, prof. Stefano Magrini, dr. Carlo Cavedon, , dr. Michele Stasi, prof.ssa Cinzia Talamonti).

Il volume include l'intervista a Nuria Jornet, chair dell'ESTRO physics committee, l'intervista alla prof. Mantanta della delegazione dei 14 colleghi Thailandesi di THASTRO che hanno partecipato al corso, gli abstract selezionati e le interviste fatte dalla dr.ssa Sara Broggi e dalla dr.ssa Elena Villaggi ai vincitori dei premi per i migliori contributi, per mostrare che dietro alle presentazioni scientifiche ci sono persone con le proprie storie e i propri interessi.

Prof. Filippo Alongi & dr. Pietro Mancosu

Responsabili scientifici convegno “SBRT: from physics to clinic”



COMUNICATO STAMPA

Parte oggi il corso sulla Radioterapia Stereotassica organizzato da AIFM e AIRO

🕒 04 ottobre 2018 16:45 📍 Sanità 📍 Firenze

Da oggi fino al 6 ottobre si terrà a Firenze la terza edizione del corso sulla SBRT (Stereotactic Body Radiation Therapy) organizzato congiuntamente dall'Associazione Italiana di Fisica Medica (AIFM) e dall'Associazione Italiana di Radioterapia e Oncologia Clinica (AIRO). Il tema di questa edizione è: "SBRT: from physics to clinic", dalla fisica alla clinica.

A testimoniare la sinergia tra queste due professioni il corso verrà aperto dai presidenti di AIRO, Prof. Stefano Magrini e di AIFM, Dott. Michele Stasi, che affermano: "Il volume ridotto da irradiare e la prossimità con organi a rischio circostanti richiedono di mantenere una precisione millimetrica per tutto il trattamento." "La tecnica SBRT rappresenta un ottimo esempio di multiprofessionalità: alle competenze cliniche dello specialista oncologo radioterapista è associato il ruolo del fisico medico."

Novità di questa edizione è l'apertura delle iscrizioni agli stranieri, che hanno risposto in gran numero: più del 20% degli oltre 200 iscritti sono stranieri, provenienti da quattro continenti. A testimoniare l'internazionalizzazione del corso interverranno anche i presidenti delle Associazioni europee di radioterapia (ESTRO, Prof. Umberto Ricardi) e fisica medica (EFOMP, Dr. Marco Brambilla). "Siamo orgogliosi di questa larga partecipazione, segno dell'eccellenza italiana in questo settore" hanno commentato i due presidenti del Congresso, Prof. Filippo Alongi e Dott. Pietro Mancosu.

Cos'è la radioterapia oncologica

La radioterapia oncologica è una disciplina clinica che si occupa del trattamento dei tumori maligni ed è impiegata nel trattamento di circa il 60% dei pazienti che ne è affetto. L'oncologo radioterapista, il medico specialista nella cura di questo tipo di tumori, si avvale non solo dei farmaci ma anche delle radiazioni ionizzanti per il loro trattamento. Per garantire il miglior percorso di cura possibile, l'oncologo radioterapista si trova spesso a collaborare con numerosi professionisti tra i quali emerge quella del fisico medico, lo specialista che si occupa della misura della dose ricevuta dal paziente e di accertarsi della qualità delle apparecchiature utilizzate per il trattamento radioterapico (fortunatamente disponibili in circa 200 Centri di Radioterapia sul territorio nazionale).

Leggi questo articolo su: <https://www.gonews.it/2018/10/04/parte-oggi-corso-sulla-radioterapia-stereotassica-organizzato-aifm-airo/>

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INTERVISTA ALLA DOTTORESSA NÚRIA JORNET

Nuria Jornet is Senior Consultant Medical Physicist in the Department of Medical Physics and Radiation Protection of Santa Creu i Sant Pau Hospital in Barcelona; Chair of the ESTRO Physics Committee, Member of the ESTRO Scientific and Education Councils and course director of the ESTRO course on Quality management: Quality monitoring and Quality Improvement.

What impressed you most about the Course on Stereotactic Body Radiation Therapy: From physics to clinic (Florence - 4-6/10/2018)?

The program was excellent and I appreciated the good balance between clinical and physics topics. Looking at the mix of physicists and oncologists that were attending the workshop was a clear sign of a programme that was of interest of all involved specialities.



Nowadays advanced technique as SBRT are no longer limited to high-qualified academic centers but they are routinely adopted in smaller and non-academic centers: how in your opinion can an association like Estro support the sharing of knowledge by centers with different experiences?

Obviously high quality training for physicists, radiation oncologists and RTTs is needed. National courses as the one organised by the Italian association is a good example. ESTRO has also a course on SBRT that is organized annually. For medical physicists a more practical course on commissioning of treatment units and TPS for stereotactic techniques would be highly appreciated by clinical medical physicists. A dosimetry audit course is now being discussed at ESTRO, auditing SBRT will be included.

The ESTRO physics workshop on science in development has also an ideal format to discuss practical issues, share experiences amongst colleagues and also the industry. SBRT could be a good topic for the 4th workshop in 2020.

What aspect of SBRT do you think can still have a greater development: technological, dosimetric, planning?

I think there is room for improvement in the three areas. Regarding technology we still need better synchronisation of imaging and delivery, imaging during beam on is still not available in most clinical treatment units. SBPT is also promising but more studies on robustness are needed to apply it safely to lung SBRT. On the dosimetry arena, several groups are showing discrepancies in the output correction factors for some detectors as proposed in TRS483 showing that still more work is needed. Regarding planning the dose prescription is still not standardised. Furthermore there is a need for solutions on dose accumulation when time resolved imaging is used.

What is the status of the transposition of Directive 2013/59 / EURATOM in Spain and how is going its implementation ?

It is still not transposed in the spanish legislation. The draft is still in the discussion phase.

Intervista alla professoressa Mantana Dhanachai

Mantana Dhanachai is associated professor in radiation oncology at Ramathibodi Hospital (Bangkok, Thailand). Her main scientific interest are: SBRT, radiosurgery and brain cancer. She was the chair of the THASTRO delegation in Florence.

What impressed you most about the Course on Stereotactic Body Radiation Therapy: From physics to clinic (Florence - 4-6/10/2018)?

The contrast of the historical, world heritage scenario of Florence and the conference venue, and the cutting edge knowledge. Unforgettable and great learning experiences!

Nowadays advanced technique as SBRT are no longer limited to high-qualified academic centers but they are routinely adopted in smaller and non-academic centers: how in your opinion can national or international associations support the sharing of knowledge by centers with different experiences?

Great opportunity and threat comes in the same coin, SBRT is very powerful but can also be very dangerous. National / international associations can help a lot with protocols, also the cohort database, so that we don't have to go through the same mistakes unnecessarily.

What aspect of SBRT do you think can still have a greater development: technological, dosimetric, planning?

All, I think.

How is the collaboration between radiotherapists and medical physicists in your country?

They have different national associations, however most of the time they have good relationship, as most of the medical physicists in Thailand have the Bachelor degree in Radiological Technology before continuing with the [M.Sc.](#) or Ph.D. in Medical Physics.



Interviste ai vincitori dei premi

Intervista alla dottoressa Emanuela Olmetto, Medico

Qual è stato il tuo percorso scolastico?

Ho conseguito la laurea magistrale in medicina e chirurgia presso l'Università Cattolica del Sacro Cuore di Roma nel 2013, discutendo una tesi sperimentale sull'utilizzo delle "piccole" dosi in associazione alla chemioterapia nel trattamento del carcinoma polmonare localmente avanzato. Ho proseguito la mia formazione specialistica presso la radioterapia dell'AOU Careggi di Firenze dove ho avuto modo di approfondire le mie conoscenze in materia oncologica sia nell'ambito clinico che nell'ambito della ricerca. Durante questi anni della specializzazione ho preso parte come sub-investigatore a numerosi



studi clinici sperimentali soprattutto riguardanti la patologia polmonare. A dicembre ho conseguito la specializzazione in radioterapia discutendo una tesi sperimentale sull'utilizzo dell'autoplanning nella radioterapia dei linfomi mediastinici. Una parte del mio percorso formativo l'ho svolta in Francia presso la radioterapia dell'istituto Marie Curie di Parigi, esperienza che è stata per me molto formativa in una città viva e stimolante. Ammetto che gli anni della specializzazione sono stati molto impegnativi, ma allo stesso tempo mi hanno permesso di crescere non solo professionalmente ma anche umanamente insegnandomi ad affrontare situazioni difficili sempre con il sorriso sulle labbra. Di questo devo ringraziare tutti i miei colleghi di Firenze e in particolare il prof. Livi che da vicino ha seguito e guidato la formazione di tutti noi specializzandi.

Cosa fai attualmente?

In questo momento sto svolgendo un'attività di ricerca presso il reparto di oncologia polmonare dell'ospedale San Luigi di Orbassano. La patologia polmonare ha da sempre suscitato grande interesse per me e questa esperienza rappresenta una grande occasione per poter approfondire e

consolidare le mie conoscenze sui tumori dell'apparato toracico frequentando uno dei centri di riferimento in questo ambito.

Come vedi il futuro prossimo?

Nel futuro spero di poter continuare a esercitare la mia professione in Italia, cercando di integrare al meglio l'attività clinica e l'attività di ricerca. E' sicuramente un progetto ambizioso e difficile da realizzare ma non impossibile. Sono quindi fiduciosa che possano aprirsi nuove strade per i giovani neo-specialisti.

Qual è l'aspetto più attraente della professione che eserciti?

Non nascondo che la nostra professione è sicuramente diversa dalle altre e forse è diversa anche da come noi da studenti di medicina la immaginavamo. A volte stare accanto alla sofferenza delle persone ci fa stare male, e non sempre siamo in grado di affrontare il dolore o la rabbia o la rassegnazione. Più semplice è certamente gioire dei successi terapeutici, comunicare gli esiti positivi ai trattamenti e regalare momenti di speranza. Credo che questo sia uno degli aspetti più attraenti del nostro lavoro, il privilegio di stare accanto a queste persone nel momento in cui sono più fragili e in cui si sentono più sole, di fronte a una malattia che spaventa e che a volte purtroppo non lascia scampo. L'altro aspetto direi sorprendente del nostro lavoro è che nel momento in cui pensi di aver esaurito tutte le tue conoscenze su un dato argomento, questo viene stravolto e quello che credevi lo standard viene messo in dubbio da terapie nuove e più promettenti. L'ambito oncologico radioterapico è sicuramente uno degli ambiti in maggiore evoluzione e la ricerca è sempre aperta a nuove sfide e nuovi traguardi che concretamente impattano nella vita dei nostri pazienti.

Intervista al dottor Luca Nicosia, Medico

Qual è stato il tuo percorso di formazione scolastica e cosa fai attualmente?

Ho conseguito la Laurea in Medicina e Chirurgia presso l'Università Cattolica del Sacro Cuore di Roma a Ottobre 2011 e la Specializzazione in Radioterapia Oncologica presso l'Università "sapienza" di Roma, Ospedale Sant'Andrea a Luglio 2018. Ho lavorato diversi anni come medico d'Emergenza in Ambulanza.

Attualmente lavoro come Dirigente Medico presso il Dipartimento di Radioterapia Oncologica Avanzata dell'Ospedale Sacro cuore di Negrar e mi occupo principalmente di patologia polmonare, gastroenterica e urologica.

Come vedi il futuro e la tua professione?

Ho una visione abbastanza ottimistica del futuro e voglio concentrarmi ancora di più sull'aspetto scientifico della mia professione, senza trascurare la parte clinica e il rapporto con il paziente.

Ciò che mi affascina di più della Radioterapia Oncologica è la sua trasversalità, a metà strada tra l'oncologia, la chirurgia e la radiologia. L'utilizzo ai massimi livelli della tecnologia e l'ampio spazio per la ricerca, sia in ambito clinico, che tecnico che biologico. Il fatto di vedere giornalmente i pazienti nel corso delle sedute di trattamento permette anche di curare molto il rapporto medico-paziente, alla base della pratica medica.



Intervista al dottor Jacopo Di Muzio, Medico

Qual è stato il tuo percorso scolastico?

La mia passione per la medicina è iniziata già dall'infanzia, quando il medico era un super eroe vestito di bianco e con mille risorse. In seguito, a partire dalle scuole superiori, ho indirizzato i miei studi verso un percorso scientifico ad impronta biologica, volto ad approfondire i principali aspetti della vita, partendo dalle piccole molecole fino alla comprensione dell'organismo in toto. Gli anni dell'università sono stati il momento cruciale per questo lungo percorso; durante questo tempo ho potuto conoscere innumerevoli autorevoli figure con molta esperienza nel campo della



medicina che hanno stimolato progressivamente la mia scelta del percorso futuro. Al V anno di studi, dopo aver dato l'esame di Diagnostica per immagini e Radioterapia, mi sono trovato a dover scegliere un tirocinio libero volto ad approfondire un argomento specifico. Essendo fresco di studio e appassionato sia di oncologia che di tecnologia decisi di frequentare l'Istituto di Radioterapia dell'Università degli Studi di Torino. Quella scelta fu la svolta decisiva che mi portò a scegliere il percorso del Radio-Oncologo; gli anni di studi si conclusero, quindi, con una tesi sul controllo ecografico di immagine nella IGRT del carcinoma prostatico. In seguito entrai subito nella scuola di specialità di Radioterapia dell'Università di Torino sotto la guida del Professor Ricardi. Durante gli anni di specialità mi sono occupato dapprima di oncologia prostatica, proseguendo il percorso di formazione intrapreso con la tesi ed in seguito di oncologia cervico-cefalica, argomento che mi appassiona tutt'ora. Argomenti di grande interesse sono stati anche la senologia e i tumori del tratto gastroenterico. Negli ultimi anni di specialità ho approfondito l'oncologia toracica e la tecnica della SBRT in diversi distretti dell'organismo, con particolare interesse per il polmone e la sua biologia. Oltre all'attività clinica sono sempre stato affiancato nella ricerca scientifica che ha accompagnato tutto il percorso della scuola di specialità.

Cosa fai in questo momento?

In questo momento lavoro come Medico Radioterapista presso l'IRCCS di Candiolo. Tale centro rappresenta un punto di riferimento per l'oncologia Piemontese attestandosi tra le eccellenze in merito alla cura dei tumori. Il reparto di radioterapia può vantare un equipaggiamento tecnologico molto avanzato ed una équipe di medici, fisici e tecnici molto giovane e dinamica. Vista la passione degli ultimi anni sto continuando ad occuparmi di oncologia toracica e radioterapia stereotassica, partecipando ai Gruppi Interdisciplinari di Cura e portando avanti progetti di ricerca. Oltre a ciò mi occupo di senologia, argomento di grande interesse per l'Istituto, di sarcomi dei tessuti molli, di ematologia e palliazione.

Come vedi il futuro prossimo?

Per quanto riguarda il prossimo futuro l'intento è quello di perseguire un'evoluzione dinamica per la mia professione, cercando di approfondire ulteriormente le conoscenze apprese fino adesso e, perché no, apprendere l'uso di nuove tecniche come la brachiterapia.

Qual è l'aspetto più attraente della professione che eserciti?

Per mia grande fortuna la Radioterapia si configura come una branca della medicina in continua evoluzione clinica e tecnica. Sicuramente le innovazioni tecnologiche sono estremamente affascinanti e, spesso, molto sensazionali. Accanto a questo esiste una compenetrazione molto forte con la professione oncologica, basti pensa alle innumerevoli possibilità di combinazione terapeutica con i farmaci. La terapia a bersaglio molecolare e l'immunoterapia hanno rivoluzionato il modo di interpretare l'oncologia avendo, peraltro, forte impatto sulle indicazioni radioterapiche e questo rende necessario un costante aggiornamento. Questa passione per lo studio e per la scoperta, nuova ogni giorno, rende unico il nostro lavoro e ci porta avanti nella nostra piccola battaglia quotidiana contro il cancro. L'ultimo, ma non meno importante, aspetto estremamente affascinante della mia professione ritengo sia il rapporto con il paziente che ci permette ogni giorno di rimanere umani e non solo legati ad un mero avanzamento tecnico e tecnologico.

Intervista al dottor Marco Fusella, Fisico

Qual è stato il tuo percorso scolastico?

Dopo il liceo scientifico frequentato in Abruzzo a Chieti, mi sono trasferito a Torino per frequentare la facoltà di Fisica presso l'Università degli Studi. Durante il terzo anno del corso di laurea, grazie a dei corsi facoltativi di fisica medica e reti neurali, mi sono interessato alla Fisica Medica. Da lì ho proseguito gli studi con la laurea magistrale in fisica biomedica con una tesi sulla dosimetria in vivo in Radioterapia, per poi iscrivermi alla Scuola di Specializzazione in Fisica Medica sempre a Torino. In questi quattro anni ho svolto il tirocinio prevalentemente presso l'AOU Città della Salute e della Scienza di Torino, occupandomi quasi a tempo pieno di radioterapia, e concludendo il ciclo di studi nel 2013 con una tesi su algoritmi di registrazione deformabile delle immagini per applicazioni in Adaptive RadioTherapy.



Cosa fai in questo momento?

In questo momento sto lavorando presso l'Istituto Oncologico Veneto di Padova dove sono stato assunto a gennaio 2016, dopo una parentesi di lavoro presso l'AOU Maggiore della Carità di Novara. Anche a Padova mi occupo prevalentemente di Radioterapia occupandomi sia della routine clinica che dell'implementazione continua di nuove tecnologie e tecniche di trattamento. Nel "tempo libero" ho iniziato ad occuparmi anche di NIR in ambito sanitario.

Come vedi il futuro prossimo?

Il mio futuro lo vedo ancora a Padova, dove il rinnovamento tecnologico ancora in corso di questi anni apre prospettive di lavoro e sviluppo interessantissime. Lavorare in un IRCCS è certamente fonte di stimolo continuo e multidisciplinarietà.

Qual è l'aspetto più attraente della professione che eserciti?

Sicuramente lavorare in un gruppo in cui le professionalità permettono un confronto e crescita continua. Avere un ruolo centrale nella qualità del trattamento che verrà erogato ad ogni paziente è uno stimolo continuo allo studio e al miglioramento. Inoltre il Fisico Medico è un lavoro che ti permette ancora di “sporcarti le mani” con misure, elaborazione dati, e serate passate ad armeggiare con strumentazioni di vario tipo, un po’ come ai tempi dell’università durante i vari corsi di laboratorio!

Intervista al dottor Davide Cusumano, Fisico

Qual è stato il tuo percorso scolastico?

Ho frequentato il liceo Classico Umberto I a Ragusa e poi mi sono trasferito a Catania, dove mi sono laureato in Fisica. Per il progetto di tesi magistrale mi sono spostato a Milano, dove ho frequentato l'Istituto Neurologico Carlo Besta: lì ho capito che avrei voluto intraprendere questa professione.



Terminata la laurea specialistica, sono riuscito ad accedere alla scuola di specializzazione in Fisica Medica a Milano, dove ho trascorso tre anni splendidi. Durante il penultimo anno della scuola, a un congresso in Spagna mi sono avvicinato a uno stand del Policlinico Gemelli, che stava cercando nuovi fisici medici da inserire nell'organico.

Mi sono candidato e fortunatamente ho passato le selezioni: da quel momento ho frequentato l'ultimo anno della scuola di specializzazione viaggiando tra Milano e Roma, dove ho svolto la mia tesi.

Cosa fai in questo momento?

Oggi lavoro come fisico medico al Policlinico Gemelli e sono al terzo anno di dottorato in Scienze Oncologiche presso l'Università Cattolica del Sacro Cuore.

La mia attività giornaliera ruota attorno all'implementazione clinica di un sistema ibrido composto da un Linac e da una Risonanza Magnetica on-board. Sono molto contento di quello che faccio, si tratta di una attività che richiede tanto impegno e dedizione, ma che è davvero molto stimolante.

Il mio dottorato è focalizzato sull'analisi radiomica di immagini di risonanza magnetica, allo scopo di elaborare sistemi predittivi in grado di supportare i clinici nelle loro decisioni giornaliere.

Come vedi il futuro prossimo?

Sono dell'opinione che il lavoro di fisico medico tra 5 anni sarà completamente diverso dal lavoro che svolgiamo oggi. L'intelligenza artificiale e l'automazione stanno completamente cambiando molte professioni e tutto quello che c'è di ripetitivo nel nostro lavoro è destinato a essere rimpiazzato dalle nuove tecnologie.

Questo lascerà spazio alla creatività e alla competenza, che saranno fattori imprescindibili per i nuovi fisici medici: non voglio dire che oggi siamo incompetenti, dico solo che il valore aggiunto di un fisico medico sarà sempre di più la sua formazione, la sua conoscenza approfondita di ambiti che sono già ben conosciuti dai medici e dagli altri operatori in campo sanitario.

Per questo abbiamo bisogno di scuole di specializzazione ad alto profilo, che offrano conoscenza diretta da professionisti del settore ma che pretendano anche competenza dagli studenti, con esami rigorosi e selettivi.

La capacità di portare qualità e innovazione in tutto quello che ruota attorno alla diagnosi e alla cura dei tumori è quello che sarà richiesto al Fisico Medico del futuro.

Qual è l'aspetto più attraente della professione che eserciti?

Questo lavoro mi piace perché mi permette di sentirmi utile per gli altri: è questo, secondo me, l'aspetto più attraente della nostra professione, che dà un senso al nostro percorso di studi.

Aspiro a fare ogni giorno il mio lavoro con lo stesso entusiasmo e dedizione che vedo negli specializzandi che entrano per la prima volta nel mondo della fisica medica.

Intervista alla dottoressa Lucia Paganini, Fisico

Qual è stato il tuo percorso scolastico?

Mi sono diplomata al liceo scientifico Alexis Carrell di Milano e mi sono iscritta alla facoltà di Fisica dell'Università degli Studi di Milano, principalmente affascinata dall'astronomia e l'astrofisica. Quando sono arrivata al terzo anno di università più che il corso di astrofisica mi avevano molto interessata un laboratorio e un corso che trattavano dell'interazione della radiazione con la materia. Per questo ho deciso di fare la tesi triennale in quest'ambito, occupandomi della caratterizzazione del fascio di neutroni di un reattore di Praga. Per la magistrale ho quindi scelto un piano di studi il più possibile nell'ambito della fisica medica. Al momento di cercare una tesi magistrale avevo due circostanze che mi spingevano: una era che a Milano non vedevo molte possibilità che mi interessassero particolarmente in università, l'altra era che il mio fidanzato viveva già da un anno a Groningen nei Paesi Bassi. Mi sono buttata e ho chiesto di poter fare la tesi all'istituto KVI di Groningen che ai tempi collaborava con l'ospedale UMCG per mettere in piedi la protonterapia. Nel 2012 mi sono quindi laureata con una tesi su metodi di caratterizzazione di materiali finalizzata alla pianificazione in protonterapia. Nel frattempo mi ero sposata e con mio marito siamo rimasti all'estero fino a metà 2014, quando abbiamo deciso di ritornare in Italia. Avevo sempre avuto l'idea di lavorare come fisica medica in ospedale e quindi ho deciso di immatricolarmi nuovamente alla Scuola di Specializzazione in Fisica Medica di Milano. Nel tempo della scuola ho eseguito il tirocinio principalmente presso l'Istituto Clinico Humanitas di Rozzano. A dicembre 2017 mi sono specializzata con una tesi intitolata: "Evaluation of an environment for Monte Carlo simulations (PRIMO) for the verification of VMAT treatment plans".

Cosa fai in questo momento?

Appena dopo la specializzazione sono rimasta nel reparto di radioterapia dell'Humanitas di Rozzano dove sono stata assunta come fisica medica. La parte principale del mio lavoro è certamente la routine clinica di pianificazione di trattamenti radioterapici e di controlli di qualità



sugli acceleratori che nel mio ospedale è molto pressante, ma trovo anche il tempo di continuare il lavoro di ricerca che ho iniziato con la tesi di specializzazione.

Come vedi il futuro prossimo?

Per quanto riguarda il mio futuro prossimo mi vedo sempre in Humanitas: ho trovato un ambiente di lavoro accogliente e giovane, con dei colleghi con cui mi trovo davvero bene e, avendo lavorato altrove in precedenza, so che questa è una cosa non di poco conto e che non voglio dare per scontata. Anche da un punto di vista professionale vedo molta possibilità di imparare nuove cose in Humanitas e questo è sicuramente stimolante e non accade in tutti gli ospedali.

Qual è l'aspetto più attraente della professione che eserciti?

Sicuramente il legame stretto che c'è tra la tecnologia e la medicina per me è molto interessante e mette insieme aspetti che mi appassionano. E poi il fatto che ci siano figure professionali diverse che devono lavorare insieme perché tutto il processo funzioni.

Abstract Clinici

Predictive factors for response and survival in oligometastatic patients treated with Stereotactic Body Radiation Therapy

D. Franceschini ¹, C. Franzese ¹, F. De Rose ¹, T. Comito ¹, G. Carta ¹, G. Radicioni ¹, GR. D'Agostino ¹, P. Navarria ¹, M. Scorsetti ¹

¹ *Radiotherapy and Radiosurgery Department, Humanitas Clinical and Research Hospital, Rozzano (Milan)*

Introduction and Aim

To evaluate patients, treatment or disease characteristics that could predict response to SBRT and survival, in order to identify candidates who will benefit from such therapy in a database of oligometastatic patients from different solid tumors.

Material and Methods

Patients treated with SBRT for oligometastatic disease between January 2014 and December 2015 were included in this analysis. Patients were defined as oligometastatic if they were affected by maximum 5 active lesions in 3 different sites. They had to be treated with SBRT with radical intent. Primary endpoint of the study was overall survival; secondary end points were local control, disease free survival and progression free survival. Local control and survival times were calculated from the day of SBRT.

Results

358 patients were included in the study. Main patients and treatment characteristics are listed in table 1. Patients received different RT schedules according to number, site and size of the metastases. Treatment was generally well tolerated, no acute or late G3-4 toxicity was recorded.

Complete response, partial response or stable disease were recorded in 152 (42.5%), 160 (44.7%) and 40 (11.1%) patients respectively. Six patients (1.7%) experienced local progression at first evaluation, while other 69 (19.6%) patients experienced local relapse during follow up. With a median follow up time of 22.2 months (range 2-49.9 months) actuarial local control time at 6, 12 and 24 months was 94.6%, 84.3% and 78.9% respectively. Distant progression was recorded in 279 patients (77.9%). Actuarial DMFS at 6, 12 and 24 months was 67.1%, 38.3% and 20.9% respectively. Actuarial PFS at 6, 12 and 24 months was 66.1%, 36.3% and 18.4% respectively.

At last follow up, 195 patients (54.5%) were still alive, in 59 cases with no evidence of disease. Actuarial median overall survival (OS) was 26.4 months, OS at 6, 12 and 24 months was 96%, 85.2% and 63.6%.

At univariable analysis sex and number of treated lesions were found to be correlated with LC. Previous medical therapies, number of treated lesions, number of involved organs, presence of inactive extratarget disease, “adjuvant” medical therapies and local response correlated with DMFS and PFS. Age at stage IV diagnosis, presence of inactive extratarget disease and local response were statistically correlated with OS.

Conclusions

SBRT for oligometastatic patients is safe and effective. Local response is strongly correlated with patients’ prognosis, underlying the relevance of local control also in a metastatic setting.

Predictive factors for oligometastatic colorectal cancer treated with stereotactic body radiation therapy.

C. Franzese ¹, T. Comito ¹, E. Toska ¹, A. Tozzi ¹, E. Clerici ¹, F. De Rose ¹, D. Franceschini ¹, P. Navarria ¹, G. Reggiori ¹, S. Tomatis ¹, M. Scorsetti ^{1,2}.

¹ *Humanitas Clinical and Research Hospital, Radiotherapy and Radiosurgery Dept, Milan-Rozzano, Italy*

² *Humanitas University, Department of Biomedical Sciences, Milan-Rozzano, Italy*

Introduction and Aim

Colorectal cancer (CRC) represents one of the major leading causes of death from cancer. Aim of the present study was to analyze pattern of care and recurrence of oligometastatic CRC patients, and to evaluate predictive factors of survival.

Materials and Methods

We included patients with a maximum of 5 metastases. Previous or concomitant systemic treatments were allowed. End points of the present study were the outcome in terms of Local control of treated metastases (LC), progression free survival (PFS), and overall survival (OS).

Results

270 patients were treated on 437 metastases (Table1). Lung was site of metastases in 48.5% of cases, followed by liver (36.4%). Systemic treatment was administered before SBRT in 199 patients (73.7%). Median follow-up time was 23 months (3 - 98.7). Rates of LC at 1, 3 and 5 years were 95%, 73% and 73%, respectively. Time from diagnosis of metastases to SBRT was the only factor predictive of LC (HR 1.62, p=0.023). Median PFS was 8.6 months. Rates of OS at 1, 3 and 5 years were 88.5%, 56.6%, and 37.2%, respectively. Lesion greater than 30 mm (HR 1.82, p=0.030), presence of metastases in organ different from lung (HR 1.67, p=0.020), the use of systemic treatment before SBRT (HR 1.82, p=0.023), and progression of treated metastases (HR 1.80, p=0.007), were all predictive of worse OS (Figure 1).

Conclusions

Stereotactic body radiation therapy represents an effective approach in the management of oligometastatic CRC. Control of treated oligometastases seems to be a strong positive predictive factor for both PFS and OS.

	N. 270 patients 437 lesions (%)
Age median (range):	69.1 (31.9 – 90.6)
<= 65	82 (30.4%)
> 65	188 (69.6%)
Sex	
Female	80 (29.6%)
Male	190 (70.4%)
PS:	
0	200 (74.1%)
1	42 (15.6%)
2	26 (9.6%)
3	2 (0.7%)
Time to metastases, median (range)	23.5 months (0 – 126.6)
<= 24 months	139 (51.5%)
> 24 months	131 (48.5%)
Site of treated metastases (per lesion)	
Lung	212 (48.5%)
Liver	159 (36.4%)
Lymph nodes	54 (12.4%)
Adrenal glands	8 (1.8%)
Bones	2 (0.5%)
Pancreas	2 (0.5%)
Number of treated organ	
1	237 (87.8%)
≥ 2	33 (12.2%)
KRAS status	
Wild type	44 (16.3%)
Mutated	62 (23%)
Unknown	164 (60.1%)
CTV mm (range):	23 (9 – 71 mm)
<=30	317 (72.5%)
>30	120 (27.5%)
Systemic therapy before SBRT	

No	71 (26.3%)
Yes	199 (73.7%)
Systemic therapy after SBRT	
No	202 (74.8%)
Yes	68 (25.2%)
Lines of systemic therapies before SBRT	
0	71 (26.3%)
1	83 (30.7%)
2	72 (26.7%)
≥ 3	44 (16.3%)
Time from metastases to SBRT median (range)	
≤ 12 months	10 (0 – 157.7)
> 12 months	154 (57%)
	116 (43%)
Total dose Gy, median (range)	
≤ 60 Gy	48 (25 – 75)
> 60 Gy	332 (76%)
	105 (24%)
Dose per fractions Gy, median (range)	
≤ 12 Gy	12 (5 – 30)
> 12 Gy	278 (63.6%)
	159 (36.4%)
Number of fractions, median (range)	
	4 (1 – 8)
BED10 Gy, median (range)	
≤ 100 Gy	105.6 (37.5 – 262.5)
> 100 Gy	94 (21.5%)
	343 (78.5%)

Table 1 Patient's, disease's and treatment's characteristics

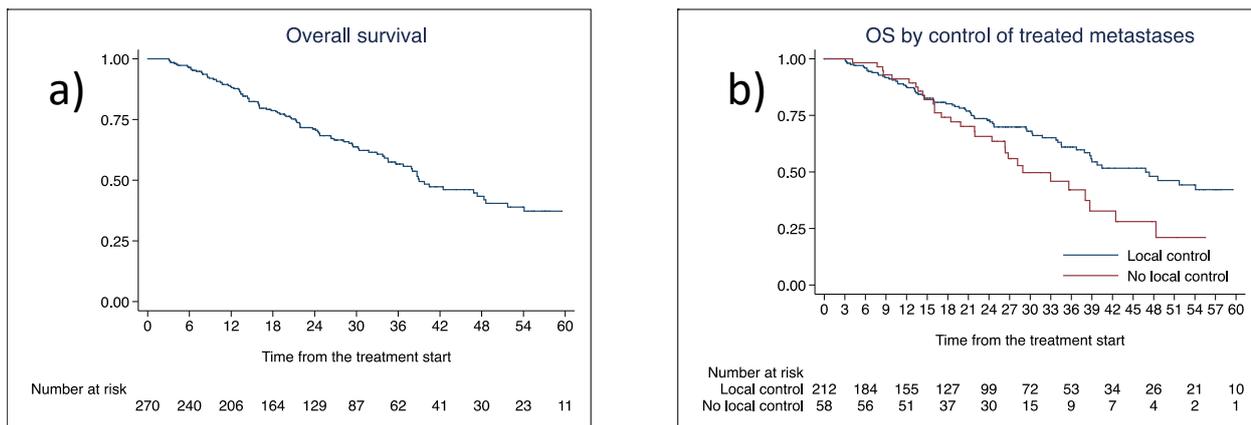


Figure 1 Kaplan-Meier curves of Overall Survival for all patients (a) and according to control of treated metastases (b)

SBRT for Liver Metastases: Results on 374 Treated Lesions

C. Menichelli¹, G. Pastore¹, A. Fanelli¹, E. Lombardo¹, F. Casamassima¹

¹*Department of Radiation Oncology, Research Institute "ECOMEDICA", Empoli, Italia.*

Introduction and Aim

The liver is a common site of metastatic spread for solid tumor and often represents the only site of metastases. Some patients are not fit to surgery excision or other tumor ablation strategies (eg. RFA) considered for limited disease. The purpose of this study is to assess the efficacy of SBRT, as ablative therapy, to achieve local control and its relationship with type of primary tumor, dose prescription and treatment delivery modalities

Materials and Methods

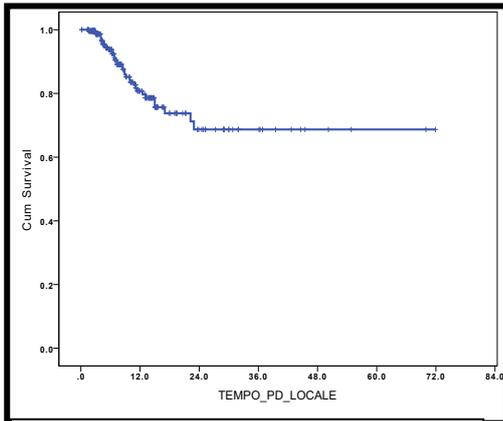
192 Patients (pts) (374 lesions) were treated by SBRT for liver metastases (primary was colon in 100 cases, breast in 29 and others in 63). Adopted inclusion criteria were no more than 5 mets and no more than 6 cm in diameter. GTV was countered using CT data sets acquired at different respiratory phases to obtain an ITV in 15/192 pts and in 110/192 pts using Active Breathing Coordinator (ABC), both during CT acquisition and treatment delivery, to achieve a reduction of respiratory displacements, in 67/192 pts using breath hold technique. In 165/192 pts gold fiducial markers as target surrogate were implanted. Target mean volume was 45 cc (range 0.3-433 cc) and mean number of treated lesion was 2.2 (range 1-5). Mean dose was 35 Gy (range 26-37.5Gy) prescribed to isocenter in 59/374 lesions and to the 67-70% isodose in 315/374 lesions delivered in three fractions. Treatment was delivered by 6MV Linac using beam modulator (ELEKTA SynergyS) equipped with 4 mm MLC, through two co-planar and no coplanar arcs and in 173/374 lesions with VMAT optimization. Isocenter position was verified before each fraction using CBCT co-registered to planning CT on diaphragm profile or gold fiducials. Local Control (LC), defined as no tumor regrowth in the irradiated volume, was evaluated by multiphasic CT at 2, 6, 12 months after SBRT and every 6 months successively. Toxicity was evaluated according to CTCAE scale.

Results

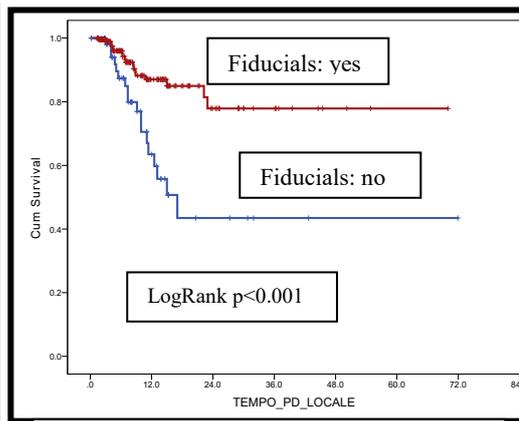
Median follow up was 16.5 months (range 3.8-87 months). The rate of LC at 6, 12, 24 months was 94 %, 81%, 70 % respectively, LC appears to be stable from two years onwards. On univariate analysis implanted fiducials (p=0.001), low lesion volume (p=0.002), higher delivered dose BED₁₀ >100 (p=0.001) were correlated with better LC. On Multivariate analysis better LC was statistically related to the use of fiducial markers (p< 0.004) and low target volume (P<0.023). No correlation was observed with tumor type, although there was a positive trend for breast secondary lesions. G1 toxicity in 13/192 patients and G2 (ulcera medically recovered) in 4 patients was observed.

Conclusions

In our experience, SBRT for liver metastasis, as ablative treatment, lead to high rate of LC that remains stable after two years (70%). The use of target surrogates improve LC rates (LC 87% vs 66% at 12 months). These results and low toxicity suggest the SBRT as a safe and effective treatment modality that can be offered to patients not suitable for other local ablative therapies.



Local Control (kaplan-Meier): 374 lesions



Local Control (kaplan-Meier): 374 lesions

Stereotactic Radiosurgery plus Immunotherapy or Targeted Therapy for brain metastases from NSCLC

E. Olmetto ¹, C. Delli Paoli ¹, L.P. Ciccone ¹, M. Perna ¹, R. Grassi ¹, E. Scoccimarro ¹, S. Scoccianti ¹, D. Greto ¹, I. Desideri ¹, G. Simontacchi ¹, L. Marrazzo ², C. Arilli ², M. Casati ², A. Compagnucci ², G. Pecchioli ³, S. Pallotta ², L. Livi ¹

¹ *Radiation Oncology Unit, University of Florence, Florence, Italy*

² *Medical Physics Unit, University of Florence, Florence, Italy*

³ *Neurosurgery Unit, University of Florence, Florence, Italy*

Introduction and Aim

Immunotherapy (IT) and Targeted Therapy (TT) have strongly changed the therapeutic management of Non-Small Cell Lung Cancer (NSCLC) patients. Radiosurgery (RS) is very effective in achieving local control of brain metastases (BM); moreover, it may have a symptomatic effect by reducing or preventing neurological deficits, in order to maintain a good quality of life longer. So far, data regarding the interactions between these novel drugs and RS in terms of efficacy and toxicity are not available. Aim of the present study is to evaluate outcome and safety of RS delivered in association to IT or TT for BM from NSCLC.

Materials and Methods

We retrospectively analysed data from NSCLC patients with BM treated with RS plus IT or TT. We selected patients who received IT or TT within 4 weeks before or after RS. RS were performed with Gamma-Knife. Clinical toxicity was evaluated according to CTCAE v.4. During follow-up, all the patients underwent contrast-enhanced brain MRI every 3 months for the first year after RS, every 4 months thereafter. Local progression-free survival (L-PFS) was defined as the time from RS to radiological progression at the site of the treated lesion, while intracranial progression at a different site, defined as distant-PFS (D-PFS), was the time interval from RS to the appearance of new BM.

Results

We selected 30 patients treated at our centre from 2012 to 2018. There were 16 women (53%) and 14 men (47%) with a median age of 63.6 years (range 47-82). All patients were affected by adenocarcinoma; 13 (43%) were EGFR-mutated, 4 (13%) were ALK-rearranged and 4 (13%) were PD-L1 over-expressed. Eighteen patients (60%) had metastatic disease when the lung tumor was newly diagnosed; among these, 10 patients (33%) had BM. At the time of RS, the majority of patients had a KPS of 90-100%, the median GPA-score was 2.5, while the median RPA-class was 1.5. The median number of treated lesions was 3 (range 1-11). Most of the patients (n=21, 70%) received a single-fraction of 24 Gy, whereas the others were treated with a dose of 18 or 21 Gy. IT

and TT consisted of Pembrolizumab (4), Nivolumab (2), Erlotinib (11), Gefitinib (4), Crizotinib (3), Ceritinib (1), Alectinib (1), Afatinib (1), Lorlatinib (1), Nintedanib (1), Rociletinib (1). IT or TT was started after the completion of RS in 9 patients; in the remaining cases (n=21), IT or TT was begun before RS (IT or TT was interrupted for a median period of seven days from RS n=10; IT or TT was continued according to the original schedule n=11). Median follow-up was 11 months. One patient developed G1 radionecrosis after 18 months from RS. No G3 toxicity was observed. Median L-PFS and D-PFS were 10.6 and 7 months, respectively.

Conclusions

RS for BM may be safely associated with IT or TT in patients with NSCLC. Prospective studies are needed to confirm our results.

Local ablative SBRT for nodal metastases of prostate cancer

A. Fanelli ¹, C. Menichelli ¹, E. Lombardo ¹, G. Pastore ¹, F. Casamassima ¹

¹ *Department of Radiation Oncology, Ecomedica, Empoli*

Introduction and Aim

Nodal recurrences as the only site of disease relapse is a common evaluation of prostate cancer after curative treatment of the primitive. When the lymph node site number involved is limited (oligometastatic status), an ablative therapy of lymphnode relapses may lead to a new phase of remission of the disease, delaying the start of hormone therapy. We examined the results in term of Local Control (LC), toxicity and Disease Free Survival (DFS) using SBRT as ablative treatment.

Materials and methods

Between 2012 and 2018 a total of 63 patients with 113 isolated lymph nodes were treated. 8 patients were initially treated with radiotherapy, 13 pts underwent a prostatectomy, 27 pts were treated with surgery and radiotherapy, 4pts received hormone therapy, 8pts hormone and radiotherapy and finally 3pts underwent surgery and then hormone therapy. All patients underwent choline-PET scan before SBRT. Dose prescription was based on lesion size and location with the median dose of 30 Gy in 3fx to 70% isodose (total dose to isocenter was 42.8 Gy, BED3=103.8). The sites of treatment included abdomen in 28.3%, pelvic 58.4%, thorax 8.55%, supra clavicular 4.75%. Median target volume was 3.18 cc (range 1.15 -5.33). Stereotactic body radiation therapy with 6 mV photons was administered using beam modulator Linac with 4mm MLC. Patient set-up and isocenter position were controlled before each fraction by CBCT. Toxicity was evaluated according to CTCAE v. 4.0 and the treatment response was evaluated by Choline PET or TC scan and PSA dosage 2 month after treatment and then every 3 month.

Results

Median follow-up was 38 months (range 2-68). 76% pts were still alive, 22% was dead and 2 % was lost in FU. 15.9% of pts relapsed out of treated field (4pts in bone and 6 lymph nodes). DFS, OS and LC at 2 and 5 years were 50%, 92% and 98%, and 17% 58% and 92% respectively. Any severe acute or late GI and/or GU toxicity (>G3) was not observed but only mild GI late toxicity in 6% of patient.

Conclusions

SBRT seems to be safe, effective, and minimally invasive in the eradication of limited nodal recurrence from oligometastatic prostate cancer. SBRT is well tolerated by patients with low toxicity and yielded a local control of the disease. SBRT could be considered as a possible alternative treatment able to preserve and/or postpone the systemic treatments or androgen

deprivation therapy in patients with isolated relapse of disease. Choline-PET scan is useful diagnostic option in order to detect both disease progression to lymph-node sites and to evaluate the results of SBRT

CyberKnife^R radiotherapy for spinal metastases from Renal Cell Carcinoma. A retrospective experience.

E. Olmetto ¹, C. Muntoni ¹, M. Lo Russo ¹, A. Peruzzi ¹, G. Stocchi ¹, G. Caramia ¹, V. Di Cataldo¹, G. Francolini ¹, B. Detti ¹, L. Livi ¹

¹ *Department of Radiation Oncology, University of Florence, Azienda Ospedaliero-Universitaria Careggi*

Introduction and Aim

Renal Cell Carcinoma (RCC) is usually considered a radio-resistant tumor. Data from literature demonstrated that alpha-beta ratio for specific RCC cell lines is low, confirming only a moderate sensitivity to RT. In this setting, use of Stereotactic Radiotherapy (SRT) to deliver high doses per fraction could increase tumor cell killing and improve local control of metastatic lesions located in critical sites [1]. The primary objective of this study is to evaluate the efficacy of SRT performed with CyberKnife^R in terms of local control in patients affected by spinal metastases from RCC. Moreover, data about Pain relief in symptomatic patients and radiation-associated toxicity are reported.

Materials and methods:

We retrospectively reviewed Data about 21 patients with 39 spinal metastases from RCC, treated with CyberKnife^R robotic system radiotherapy between January 2015 and June 2017. The total dose delivered ranged between 18 Gy and 30 Gy in in 3-5 fractions. Disease control was evaluated through CT scan performed every 3 months. Data about pain relief in symptomatic patients and radiation-associated toxicity according to CTCAE v 4.03 scale were collected and reported.

Results

Median follow up was 9.8 months (SD: 10.7; range 3-36.6 months). The mean age at RT was 63.5 years (range: 35–83 years). Sixteen out of 21 patients (16.2%) were symptomatic for pain at baseline. Local control was achieved in 19 patients (90%). Distant progression (defined as progression out of irradiated volume) occurred in 11 patients (52%). Average progression-free survival time after radiotherapy was 6.1 months (SD 6.1; range: 0.8-16.2). Pain relief was achieved in all symptomatic patients. Only one patient reported G2 acute gastrointestinal toxicity.

Conclusions

Cyberknife^R robotic radiotherapy showed excellent results in terms of local control and pain relief in this population. Prospective data are needed to compare this treatment strategy with conventional radiotherapy

Gender	
Male	12 (62)
Female	9 (38)
Age at SRS (y)	
Median	63.4
Range	35-81
Nephrectomy	
Yes	17 (80)
No	4 (20)
Histological examination	
Clear cell carcinoma	17 (80)
Others	4 (20)
Metastases	
Single	4 (19)
Multiple	17 (81)
Symptoms	
Yes	16 (76)
No	5 (24)
Mean target volume (range)	74cm ³ (5,76 – 481,95)
Dosimetric data:	
<i>Mean PTV Coverage (%)</i>	<i>90,7 (81,24 – 98, 61)</i>
<i>Mean Spinal cord Dmax(Gy)</i>	<i>11.49 (0.01 – 18.01)</i>
<i>Mean Cauda Dmax(Gy)</i>	<i>9.96 (0.4 – 22.67)</i>

Table 1. Baseline features of study population and summary of dosimetric data from treatment plans.

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Stereotactic radiotherapy in oligometastatic urothelial cancer patients: a retrospective experience.

G. Caramia ¹, A. Peruzzi ¹, M. Lo Russo ¹, C. Muntoni ¹, G. Stocchi ¹, L. Visani ¹, V. Di Cataldo ¹, G. Francolini ¹, B. Detti ¹, L. Livi ¹

¹ *Department of Radiation Oncology, University of Florence, Azienda Ospedaliero - Universitaria Careggi*

Introduction and Aim

Patients affected by urothelial cancer often recur after local surgery, with distant metastases representing up to 90% of relapses. Metastatic disease is detected at diagnosis in 4% of patients. After relapse, few therapeutic options are available, with a median overall survival of 9 to 15 months. Highly selected patients with low burden of disease may benefit from local treatment of metastatic sites. In this setting Stereotactic Body Radiation Therapy (SBRT) could increase local control and improve patients outcome [1]. We retrospectively reviewed data from patients treated with SBRT in our institution for metastases from urothelial cancer, to analyze efficacy and toxicity of this approach.

Materials and Methods

We retrospectively collected data from clinical records of 19 patients treated in our institution since May 2011 to October 2017 with SBRT for oligometastatic recurrence after local surgery or oligoprogression during systemic therapy for urothelial carcinoma (≤ 3 metastatic lesions). Simple descriptive statistics were used to analyze local control (LC), response rate, symptoms control, progression free and overall survival (PFS and OS), measured from the start of treatment to progression or death from any cause. Acute and late adverse events were reported according to CTCAE v 4.03.

Results

Nineteen patients were treated on 25 metastatic lesions; 5 of them received treatment on multiple sites. Median age at treatment time was 71 years. Primary tumor sites were bladder (78,9%), kidney pelvis (15,8%) or urethra (5,3%). Majority of patients had received radical surgical treatment of primary tumor. Only one patient was metastatic at diagnosis, and received surgery as a primary treatment. After an average follow up of 11.5 months, LC was achieved in 17 lesions (68%). Complete response, partial response and stable disease was reported 2 (8%), 8 (32%) and 7 (28%) treated lesions, with an overall response rate of 40%. Of note, no local recurrence or progression was noticed during follow up in lesions with complete or partial response. Average overall survival

(OS), was 13.8 months. Only 3 patients reported \leq G2 adverse events, consisting of asthenia, dysphagia and nausea.

Conclusions

SBRT for local treatment of oligometastatic or oligoprogressive disease can be effective and safe in selected patients. Prospective studies are needed to find correct selection criteria and optimal dose and fractionation.

Mean age (years)	70.2
Primary tumor sites (%)	Bladder: 15 (78,9%) kidney pelvis: 3 (15,8%) urethra: 1 (5.3%)
Chemotherapy (%)	No Chemotherapy: 9 (47,4%) CDDP/CBCDA plus Gemcitabine: 10 (52,6%)
Median prescription RT dose (Gy)	33 (18-60)
RT fractionation (number of fractions)	1-8
RT technique (%)	Cyberknife® 12 (63.1%) VMAT 7 (36.9%)
Lesions localization (%)	Bone :5 (20%) Lymph nodes: 8 (32%) Local recurrence: 2 (8%) Brain: 3 (12%) Liver: 2 (8%) Lung: 5 (20%)
Results	Mean Overall survival: 13.8 months Local control: 68% Overall response rate: 40% Adverse events: <ul style="list-style-type: none"> ● Asthenia: 1 (G1), 1 (G2) ● Nausea: 2 (G1) ● Dysphagia: 1 (G1)

Table 1. Patients and treatment characteristics. Note: CDDP: Cisplatin; CBCDA:Carboplatin; Gem:Gemcitabine; RT: Radiotherapy; VMAT: Volumetric Modulated Arc Therapy

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Re-irradiation of recurrent glioblastoma using helical TomoTherapy with simultaneous integrated boost: preliminary considerations of efficacy

D. Arpa ¹, A. Savini ², G. Ghigi ¹, E. Parisi ¹, S.P. Colangione ¹, L. Tontini ¹, M. Pieri ¹, R.S. Bellia ¹, E. Neri ¹, S. Micheletti ¹, A. Sarnelli ², A. Romeo ¹

¹*Radiotherapy Unit, Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, Meldola, Italy*

²*Medical Physics Unit, Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, Meldola, Italy*

Introduction and Aim

There is still no standard treatment for recurrent glioblastoma multiforme (GBM). However, re-irradiation may be a therapeutic option. We re-irradiated recurrent glioblastoma using image-guided helical TomoTherapy with simultaneous integrated boost (SIB) technique. The purpose of this retrospective study was to evaluate the efficacy and safety of this treatment.

Material and Methods

Between August 2008 and February 2018, 26 patients with recurrent GBM underwent salvage radiotherapy (RT) using helical TomoTherapy with SIB. All patients had previously been treated with a standard dose schedule of 60 Gy in 30 fractions. The planning target volume (PTV) was delineated on the area of peritumoral edema using T1, T2 and flair magnetic resonance imaging (MRI)-sequences as the area of suspected tumor diffusion. The PTV-boost was defined as the tumor visible on enhanced T1-MRI. The median PTV was 112 cc (range 9.8-395 cc) and the median PTV-boost was 33 cc (range 6.7-194 cc). Median prescription doses were 20 Gy (range 12-20 Gy) to the PTV and 25 Gy (range 15-25 Gy) to the PTV-boost in 3-5 fractions. Prescribed dose isoline to the PTV-boost was 67% (*i.e.* maximum dose within the PTV-boost was in the range of 22.5-37.5 Gy). Treatment toxicity was evaluated by converting the 3D-dose distribution to the equivalent dose in 2 Gy fractions (EQD2) on a voxel-by-voxel basis.

Results

The median interval between primary RT and salvage RT was 18.7 months (range 3.6-64.8 months). Median follow-up from re-irradiation was 27.8 months (range:1.6-88.5 months). Median overall survival of re-irradiated patients was 9.5 months (95% CI: 6.8-11.3 months). The maximum and average EQD2 to the healthy brain of re-irradiation was within the range 35.3-75.6 Gy (median 53.0 Gy) and 1.0-13.7 Gy (median 6.1 Gy), respectively. All patients completed the radiotherapy and none had clinically significant acute toxicities.

Conclusions

Our results suggest that helical TomoTherapy with the proposed SIB technique could be a safe and feasible treatment option for patients with recurrent GBM, even those with large tumors. Overall survival was comparable with that of other re-irradiation protocols of stereotactic radiotherapy.

30 Gy single dose Stereotactic Body Radiation Therapy (SBRT) in a series of patients affected by early-stage NSCLC

L. Nicosia¹, C. Reverberi¹, L. Marinelli¹, L. Agolli², V. De Sanctis¹, M. Valeriani¹, M.F. Osti¹

¹ *Department of Radiation Oncology, Sant'Andrea Hospital, "Sapienza" University of Rome, Italy*

² *Department of Radiation Oncology, Faculty of Medicine and University Hospital Carl Gustav Carus, Technische Universität Dresden, Germany. OncoRay - National Center for Radiation Research in Oncology, Dresden, Germany*

Introduction and Aim

To evaluate local control (LC), survival and long term adverse effects in a series of patients with early-stage NSCLC who received 30Gy in single dose with stereotactic technique.

Materials and Methods

Between December 2008 and September 2018 a total of 55 patients affected by early stage NSCLC were treated at our Institution. All 55 lesions were treated with a 30 Gy single dose stereotactic body radiotherapy (SBRT). Forty-eight (87.2%) tumors were stage IA and 7 (12.8%) were stage IB. Prognostic factors were also assessed.

Results

The median follow-up was 39 months. Local progression occurred in 5 (9%) lesions after a median time of 28.2 months. Intra-thoracic progression (new lung lesions or thoracic lymph node metastases) occurred in 3 (5.4%) patients, two (3.6%) of which had nodal metastases to the omolateral hilar station. Ten (18%) patients had distant progression in association or not to other sites of relapse after a median time of 21.8 months. The 3- and 5-years local progression-free survival (LPFS) were 85.7% and 77.3%, respectively. Two (3.6%) patients had grade 3 pneumonitis. Fifty-three patients were evaluated for late toxicity (follow-up >6 months): 14 (25.4%) had grade ≤ 2 fibrosis, 1 (1.8%) experienced grade 3 fibrosis. Median OS was 42 months. At the univariate analysis, $PTV \leq 16$ cc correlated significantly with a longer LPFS ($p=0.001$) and OS ($p=0.02$). At the multivariate analysis, $PTV \leq 16$ cc was predictive for longer LPFS ($p=0.006$).

Conclusions

Our results confirm the effectiveness and safety of this schedule administered in selected patients. Further prospective series could better validate these results and could investigate the safety of this schedule in selected candidates.

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Efficacy and safety of Stereotactic Body Radiation Therapy SBRT with concurrent Trabectedin in metastatic soft-tissue sarcoma patients. A single Institution experience

D. Pezzulla ¹, M. Lo Russo ¹, S. Lucidi ¹, V. Maragna ¹, M.A. Teraica ¹, D. Greto ¹, I. Desideri ¹, G. Francolini ¹, L. Livi ¹

¹ *Department of Radiation Oncology, University of Florence, Azienda Ospedaliero - Universitaria Careggi*

Introduction and Aim

The aim of this observational monocentric study is to assess the efficacy and safety of Trabectedin administered concurrently with stereotactic body radiation therapy (SBRT) in patients with metastatic soft-tissue sarcomas (STS).

Materials and Methods

Twelve metastatic STS patients treated with SBRT to metastatic sites and concomitant Trabectedin between 2009 and 2017 were retrospectively analyzed. Trabectedin dose was 1.5 mg/m² in 24-hour infusion every 3 weeks. SBRT was performed within 5 weeks from last Trabectedin infusion with Volumetric Modulated Arc Therapy (VMAT); dose prescription was prescribed depending on tumor site and size. Overall response rate was assessed using Response Evaluation Criteria in Solid Tumors version 1.1. For clinical evaluation, we used Numerical Rating Scale (NRS) for pain response, Common Terminology Criteria for Adverse Events scale version 4.03 and RTOG Common Toxicity Criteria for radiation adverse events.

Results

The median age at diagnosis was 47.5 years (range 19-68). Histopathologic subtypes were leiomyosarcoma (33.3%), spindle and pleomorphic sarcoma (25%), synovial sarcoma (8.3%), pleomorphic liposarcoma (8.3%), pleomorphic sarcoma (8.3%), spindle sarcoma (8.3%), malignant peripheral nerve sheath tumor (8.3%). Eight (66.7%) patients underwent neoadjuvant and/or adjuvant treatments, 4 (33.3%) patients had metastatic disease at diagnosis. Mean number of prior chemotherapy lines for metastatic disease was 1 (range 0-2). The median number of cycles received before SBRT was 2.5 (range 0-9). Metastases sites treated included bone (50%), soft tissue (25%), lung (16.7%), lymph nodes (8.3%); in seven patients (58.3%) lesions were painful and the mean NRS before SBRT was 5.28 (range 2-8). Anemia was the most common ≥ 3 grade hematologic toxicity (25%) followed by thrombocytopenia (8.3%) and elevated transaminase (8.3%). Incidence of ≤ 2 grade radiation dermatitis was of 16.6%; no ≥ 3 grade radiation toxicities were reported. One pathologic bone fracture was experienced. At a median follow-up of 39.4 months, 9 patients (75%) had a stable disease (SD) and 3 patients (25%) had a progressive disease (PD). The median time to

progression (TTP) was of 34 months. At clinical evaluation three months after SBRT the median NRS was 1.85 (range 0-4).

Conclusions

Our experience demonstrated that SBRT associated with trabectedin, in patients with metastases from STS, increase the local metastases control with a favorable safety profile.

Cyberknife radiosurgery for primary or secondary orbital lesions: a single- centre experience

L. Visani ¹, I. Desideri ¹, G. Francolini ¹, V. Di Cataldo ², L. Masi ², I. Meattini ¹, M. Loi ¹, D. Greto ¹, M. Lo Russo ¹, R. Grassi ¹, M.A. Teriaca ¹, P. Garlatti ¹, G. Simontacchi ¹

¹ *Department of Experimental and Clinical Biomedical Sciences, Radiation Oncology Unit, University of Florence - Azienda Ospedaliero-Universitaria Careggi.* [L]
[SEP]

² *CyberKnife Center, Istituto Fiorentino di Cura ed Assistenza, Florence, Italy*

Introduction and Aim

Orbital lesions are rare, but are likely to become symptomatic and can impact on patients' quality of life. Local control is often difficult to obtain, because of proximity to critical structures. Cyberknife^R stereotactic robotic radiotherapy could represent a viable treatment option.

Materials and Methods

Data of patients treated for intraorbital lesions from solid malignancies were retrospectively collected. All patients underwent treatment with Cyberknife^R system (Accuracy Inc., USA). We analyzed local control (LC), response rate, symptoms control, PFS and OS, acute and late toxicity.

Results

From January 2012 to May 2017, 20 treatments on 19 patients were performed, with dose ranging from 24 to 35 Gy in 1-5 fractions, prescribed at an average isodose line of 79.5% (range 78-81). After a mean follow up of 14.26 months (range 0-58), overall response rate was 75%, with 2 and 4 patients presenting a partial and complete response, respectively. Mean time to best measured response was 15.16 months (range 2-58). Thirteen patients were alive, with a local control rate of 79%. Mean time to local progression was 5 months (range 3-7). Three patients reported improvement of symptoms after treatment. Mean PTV dose coverage was 97.2% (range 93.5-99.7). Mean maximum dose (Dmax) to eye globe, optic nerve, optic chiasm and lens was 2380.8 cGy (range 290-3921), 1982.2 cGy (range 777.3-2897.8), 713.4 cGy (range 219.5-2273) and 867.9 cGy (range 38-3118.5). Four patients presented acute toxicity.

Conclusions

This current retrospective series demonstrated that Cyberknife^R robotic stereotactic radiotherapy is a feasible and tolerable approach for intraorbital lesions.

Stereotactic body radiotherapy for oligometastases: systematic and random errors from 347 image registrations

S. Borghesi ¹, C. Gasperi ², E. Tucci ¹

¹*Azienda USL Toscana sud est, Radiotherapy Unit, San Donato Hospital, Arezzo*

²*Azienda USL Toscana sud est, Health Department Staff, Medical Physics Unit, San Donato Hospital, Arezzo*

Introduction and Aim

Stereotactic Body Radiotherapy (SBRT) involves the delivery of high biological equivalent doses in a small number of fractions for the management of oligometastases. Accurate target localization with image guidance such as onboard ConeBeam Computed Tomography (CBCT) before treatment delivery is therefore essential, as small changes in patient position can confer significant dosimetric impact on adjacent structures and on target coverage.

Materials and Methods

Set-up errors for 62 oligometastases in 56 patients consecutively treated with SBRT using Volumetric Modulated Arc Therapy (VMAT) were assessed using CBCT at the Radiotherapy Unit of San Donato Hospital – Arezzo. In 20 cases SBRT was delivered to abdominal metastases (5 bone, 15 lymph nodes), in the remaining 42 to thoracic metastases (7 bone, 32 lung, 3 lymph nodes). Positional error was online -corrected in x, y and z translational planes and rotational axes using a robotic couch, applying 2 mm and 2° action levels. Systematic and random setup errors were calculated for these anatomic sites. All patients were treated with VMAT using two co-planar arcs to achieve the goal of at least 95% of the PTV volume covered by at least 95% of the prescribed dose while limiting dose to normal structures. Prescribed doses included 30 – 48 Gy delivered in 3 to 5 fractions.

Results

Two hundreds fifty-eight fractions of SBRT were delivered with 347 image registrations and on line correction. Across all fractions, the mean positional error for abdomen was greatest in the x translational plane (1.2 mm±4.9 mm) and y rotational axis (0.54°±1.26°), while for thorax in the z translational plane (-1 mm±4.6 mm) and y rotational axis (-0.18°±1.57°). The systematic translational setup errors were -1.2 mm±4 mm, 0.4 mm ±3.8mm, and 0.4 mm±3.1 mm for abdomen, and -0.8 mm±2.6 mm,-0.8 mm ±3.3 mm and -1 mm±3.8 mm for thorax for x, y, z, respectively. The random translational setup errors were 3.1 mm, 5.1 mm, and 3.6 mm for abdomen, and 2.5 mm, 2.9 mm, and 3.4 mm for thorax. The systematic rotational setup errors were -0.57°±2.1°, 0.54°±0.97°, and 0.22°±0.91° for abdomen, and -0.1°± 1.1°, -0.19°±1.2° and -

$0.11^{\circ} \pm 1.1^{\circ}$ for thorax. Random rotational setup errors were 1.04° , 0.87° and 0.87° for abdomen, and 1.07° , 1.41° and 0.91° for thorax.

Conclusions

For oligometastatic patients treated with SBRT and image-guidance, the current applied planning margins at our Institution for abdominal and thoracic target volumes appear safe.

Gammaknife radiosurgery in patients receiving anticancer immunotherapy: efficacy and safety

M. Lo Russo¹, D. Pezzulla¹, S. Lucidi¹, V. Maragna¹, M.A. Teriaca¹, C. Delli Paoli¹, E. Olmetto¹, L.P. Ciccone¹, D. Greto¹, I. Desideri¹, G. Francolini¹, M. Casati², A. Compagnucci², L. Marrazzo², C. Arilli², L.Livi¹

¹ *Radiation Oncology Unit, University of Florence, Florence, Italy*

² *Medical Physics Unit, University of Florence, Florence, Italy*

Introduction and Aim

Radiosurgery (RS) is the local standard treatment in patients with limited number of brain metastases. Immunotherapy is a novel therapeutic options in cancer treatment: in last years Immune Check-point Inhibitors (ICIs) have been introduced with unexpected prolonged survival¹. Preclinical studies suggested that radiotherapy could induce tumor immunogenicity and convert the tumor into an in situ vaccine². The aim of our study is to investigate the safety and the efficacy in terms of local control and overall survival of concurrent radiosurgery and immune ICIs in brain metastases.

Materials and Methods

Data of patients with Non Small Cell Lung Cancer (NSCLC), melanoma and renal carcinoma brain metastases treated between January 2014 and March 2018 with RS and ICIs were retrospectively reviewed. A single session of Radiosurgery was delivered using Elekta Gamma Knife Perfexion system. Concurrent immunotherapy was defined as ICIs administered within \pm 6 weeks of radiosurgery treatment, in particular patients received CTLA-4 inhibitors (Ipilimumab) or PD-1 inhibitor (Nivolumab) or both. Patients underwent clinical evaluation and gadolinium enhanced MRI 45 days after RS and every three months thereafter. Tumor response was defined according to iRANO (immunotherapy Response Assessment for Neuro-Oncology) criteria.

Results

22 patients for a total of 102 brain metastases were treated with RS and ICIs. Mean age was 58.7 years (range: 32-77). The histology of primary disease was melanoma in 11 (50%) patients, NSCLC in 8 (36.4%) and renal cell carcinoma in 3 (13.6%). Mean diagnosis-specific graded prognostic assessment score (DS-GPA) was 2.4 (range: 1-4), 1.8 (1-2.5) and 2.8 (2-3.5) for melanoma, NSCLC and renal cell carcinoma patients, respectively. Nine (41%) patients received prior whole brain radiotherapy. Nivolumab was administered in 15 (68.2%) patients. Six (27.3%) patients received Ipilimumab and one (4.5%) patient received both ICIs. Mean metastases volume was 0.240 cc (0.001-5.510). Mean prescription dose was 21.3 Gy (11-24). One (4.5%) melanoma patient treated

for 16 metastases developed seizures 21 days after treatment. Five (22.7%) patients developed radionecrosis during follow up. At statistical analysis no factors correlated to radionecrosis development. Overall survival at 12, 24 and 36 months was 63%,46.7% and 20.8%, respectively. At univariate analysis a worse prognostic factor for overall survival was GPA >1(p=0.045) not confirmed at multivariate. Local control at 3 and 6 months was 100% and 85%, respectively. Furthermore Distant brain control was 90.5% at 3 months and 80% at 6 months. A previous whole brain radiotherapy correlated with a higher risk of distant brain failure at 6 months after radiosurgery and ICIs administration (p=0.026).

Conclusions

The association of immune checkpoint inhibitors and RS is feasible and did not result in severe toxicity.

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Lung optimized treatments: evaluation of target coverage and PTV margins adequacy using Montecarlo algorithm.

A. Brogna ¹, F. Midili ¹, C. Siragusa ¹, E. Mongelli ¹, A. Micali ¹, M. Angiocchi ¹, P. Inferrera², S. Lanzafame ¹, A. Pontoriero ³, G. Iati ³, S. Pergolizzi ³, I. Ielo ¹

¹ *U.O.C. di Fisica Sanitaria - A.O.U. Policlinico "G. Martino" - Messina*

² *Scuola di Specializzazione FISICA SANITARIA Università degli studi di Messina*

³ *U.O.C. di Radioterapia - A.O.U. Policlinico "G. Martino" - Messina*

(4) Unità di Radioterapia - Marrelli Hospital- Crotone

Introduction and Aim

The purpose of this work is to evaluate the target coverage for lung tumors treated with robotic radiosurgery SBRT considering the different motion management strategies of the Lung Optimized Treatment (LOT), the choice of safety margins and the use of the Monte Carlo (MC) algorithm.

Materials and Methods

From January 2018 in our Centre twenty-eight patients with lung lesions were treated with LOTs (14 patients in the 2-view modality, 8 in the 1-view modality and 4 in the 0-view modality). The ITV was contoured by the envelope of the GTV positions both in the expiration (primary series) and in the inspiration phases. PTV margins were defined according to the tracking modality: ITV+2 mm in 2-view modality, ITV+[5-7]mm in the OUT-tracking direction and +2 mm in the IN-tracking direction in 1(A/B)-view modality, CTV+[5-7]mm in 0-view modality. For each patient, a Ray Tracing (RT) plan was computed with TPS Multiplan. Tumor dose prescribed for primary tumors was 45-60 Gy in 4 and 3 fractions respectively or 23 Gy in single fraction for lung metastasis. For each patients a clinical objective to coverage the 95% of the PTV with the prescribed dose was required. Using the same patient data, beam number, directions, weights, and monitor units, each RT plan was also re-calculated using the MC algorithm (1% uncertainty level) and the PTV/GTV coverage was evaluated.

Results

In the overall comparison, MC plans with the same prescription isodose line of the RT ones showed a PTV coverage always lower than that RT one: V100 [95-99]% vs. [58-90]% with RT and MC algorithm, respectively. In particular, lesions treated in 1/0-View modality showed the most considerable difference. Thus, in these cases, MC plans should be re-prescribed to a significantly lower prescription isodose line to obtain the same PTV coverage. The wider are the PTV margins, the greater is the collapse. In particular, in case of lesions treated with 1or 0 -view modality, a

prescription at lowest isodose line in order to ensure a GTV coverage of at least 95% seems to be more indicated.

Conclusions

MC simulates with high accuracy the condition of the lack of lateral electronic equilibrium at the interface between media with sudden relative electron density variation (hypodense lung tissue/dense nodule). The final effect is a collapse of the isodose lines on the dense tissue in the PTV, with a consequently considerable decrease of the PTV coverage. In the lesions with 1-0 view the choice to prescribe to lowest isodose line is due to the GTV displacement inside the PTV during the breath, in fact the dense nodule occupies temporarily all the PTV lung hypodense volume. Thus, MC algorithm seems to be more suitable in case of NSCLC worthy of SBRT treatment with ROBOTIC RADIOSURGERY, but GTV position, PTV margins, the respiratory excursion and not only the PTV coverage must be considered in order to operate prescriptions at lowest isodoses.

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- [5] Clinical introduction of Monte Carlo treatment planning: A different prescription dose for non-small cell lung cancer according to tumor location and size Noëlle C. van der Voort van Zyp a^{*}, Mischa S. Hoogeman a, Steven van de Water a, Peter C. Levendag a Bronno van der Holt b, Ben J.M. Heijmen a, Joost J. Nuyttens a

Improved OS in selected cohorts of oligometastatic HNSCC patients treated with lung SBRT.

C. Becherini ¹, L.Visani ¹, P. Garlatti ¹, I. Dominici ¹, V. Salvestrini ¹, LP . Ciccone ¹, M.Mariotti ¹, V. Di Cataldo ², G. Simontacchi ¹, P.Bonomo ¹, I.Desideri ¹, L. Livi ¹

¹ *Radiation Oncology Unit, Oncology Department, Azienda Ospedaliero-Universitaria Careggi, University of Florence, Florence, Italy Firenze*

² *CyberKnife Center, Istituto Fiorentino di Cura ed Assistenza, Florence, Italy*

Introduction and Aim

Main goal of palliative RT for HNC patients with metastatic disease is symptom relief or prevention of symptoms. Life prolongation could be an outcome in oligometastatic cases. Our analysis aim to explore if SBRT to metastatic sites of head and neck squamous cell carcinoma (HNSCC) might improve the progression-free survival (PFS) in oligometastatic HNSCC patients. Secondary endpoints were local control (LC), overall survival (OS) and toxicity.

Materials and Methods

We retrospectively selected 17 patients affected by oligo-metastatic HNSCC treated between April 2013 and February 2017, at the Unit of Radiation Oncology. Inclusion criteria were the following: oligometastatic HNSCC with ≤ 5 metastatic sites, PS ≤ 2 , FDG-PET/CT staging, histology confirmed through FNAB. Radiotherapy has be delivered using stereotactic body radiotherapy (SBRT) technique consisted of 45-60 Gy in 3-7 fractions. Primary end points was progression-free survival (PFS) in oligometastatic HNSCC patients. Secondary endpoints were local control (LC), overall survival (OS) and toxicity.

Results

Among the 17 HNSCC patients (1 women and 16 men; mean age 66,1 years) with lung metastatic lesion, 4 had larynx carcinoma (23,5%), 4 oropharyngeal carcinoma (23,5%), 4 hypopharyngeal carcinoma (23,5%), 2 oral cavity carcinoma (11,8%), 1 nasopharyngeal carcinoma (5,9%), 1 CUP (5,9%) and 1 squamous cell carcinoma of salivary glands (5,9%). p16/HPV status was tested only on 6 patients (4 negative and 2 positive).5 patients were metastatic “ab initio”, 7 patients presented an oligoprogressive disease while the remaining 5 patients had an oligorecurrent pulmonary disease. After a median follow-up of 33 months (range, 6-60 months),mean PFS after SBRT was 13 months. One-year after SBRT LC and OS were 90% and 100%, respectively. Two-year after SBRT LC and OS were 71,5 % and 92,3 %, respectively. At Univariate analysis Overall survival (OS) was higher for patients without “ab initio” metastatic disease (P = 0,0019, 95% CI 44,380- 59,398), but this was not confirmed at multivariate analysis. PFS post SBRT was longer both at univariate and multivariate analysis for non smoker (p=0,04 and

p=0,0438, respectively) and for patients who had primitive cancer of larynx (p=0,0007 and p=0,0263). SBRT was well tolerated, and no Grade ≥ 3 toxicity was documented. Grade 2 acute toxicity were fatigue in 2 cases and Grade 1 dyspnea in 1 case. We recorded only 1 case of late toxicity dyspnea G1.

Conclusions

Lung SBRT for selected cohorts of HNSCC oligometastatic patients is safe and feasible treatment providing an OS benefit.

SBRT for oligometastatic patients on the lung. A mono-institutional experience on 849 Treated Lesions

E. Lombardo ¹, G. Pastore ¹, C. Menichelli ¹, A. Fanelli ¹, F. Casamassima ¹

¹*Department of Radiation Oncology, Research Institute "ECOMEDICA", Empoli, Italia.*

Introduction and Aim

Patients with oligometastases to the lung from solid tumors are now considered candidates for curative therapy. Uncertainties on the patients selection and the relationship with systemic therapies are still not well defined. We study the results in terms of LC, OS, toxicity and progression modality in 409 pts treated with SBRT for pulmonary oligometastases from different primary tumors.

Materials and Methods

Between December 2010 and January 2018, 409 pts (257 male and 152 female) were treated with SBRT on 849 lesions. Primary cancer was lung in 44%, colorectal in 25%, breast in 6%, H&N in 3%, Kidney in 4% and 18% others. The histological type was Adenocarcinoma in 65%, Squamous carcinoma in 18%, other in 17%. All lesions were contoured on CT scan data sets acquired in supine position using wing board and dual legs. CT was acquired in breath hold using Active Breathing Coordinator (ABC) device in 315 pts, for 44 pts was used a 4-dimensional (4D) CT. Treatments were planned using MONACO TPS with Montecarlo optimization algorithm. Median target volume was 3,24 cc. The median dose of 33,2 Gy was prescribed to 70% isodose with median BED at the isocenter of 118Gy in 1 to 3 fx (median 3fx). Treatment was delivered by 6MV Linac with beam modulator. Set-up and isocenter position assessed by CBCT. Toxicity was evaluated using CTCAE v 4.0

Results

With median follow up of 22 months (range 3-57), median OS was 56m, DFS was 16m and median LC 18m. 38 pts relapsed in the treatment field, 91 pts in the chest and 246 showed extra pulmonary recurrences. Statistically significant differences on OS was observed between patient with primary controlled or not (2y, OS 88% vs 60%; p=0.001), with metachronous vs synchronous metastases (2y, OS 97% vs 63%, p=0.001), chemotherapy or not after SBRT (2y, OS 86% vs 52%, p=0.02). 5y OS for patients treated for breast metastases was 87%, for colorectal cancer 51% and for NSCLC 61%. No significant differences on LC was detected between different primary tumors. LC rates appear to relate only to BED value. Toxicity was mild and not exceeded the grade 2.

Conclusions

SBRT appears as safe and effective therapy showing high rate of LC of pulmonary metastases using BED value exceeding 100Gy. The influence on OS appears to be related to the time of metastases appearance (synchronous vs metachronous), primary tumor controlled or not and the use of chemotherapy after SABR. The rate of OS, confirms the possibility to use of SABR with curative intent in well selected oligometastatic patients. The better rates of OS occurs in pts treated for breast and colorectal cancer. The majority of failures was represented by extra thoracic spread, leading to necessity of more effective systemic therapies.

New prognostic factors in the stereotactic body radiation therapy treatment of early stage non-small cell lung cancer

J.Di Muzio ¹, S.Badellino ¹, M.Levis ¹ and U.Ricardi ¹

¹ *Department of Oncology, University of Torino, Torino, Italy*

Introduction and Aim

The indication of stereotactic radiotherapy in operable patients affected by early stage NSCLC who refuse surgery is always increasing, with the need to identify prognostic factors for disease control. Our study aims to identify histological and molecular biology factors for a prognostic stratification of these patients.

Materials and Methods

We retrospectively reviewed The database of the radiotherapy institute of the University of Turin was retrospectively reviewed in search of patients undergoing SBRT for early stage non-small cell lung cancer from January 2003 to October 2017. Only patients with histological typing performed at the Pathological Anatomy Service of the University of Torino were included in the analysis. Patient and tumor data were collected together with immunohistochemistry and molecular biology data. Molecular biology data detected were EGFR mutation, ALK translocation, KRAS, ROS1 and BRAF mutation. the patients were analysed according to the subdivision into 3 groups. The first with the only KRAS positive, the second (unfavorable) with KRAS positive, ROS1 negative and BRAF positive, the third (very unfavorable) with the presence of the previous factors but EGFR and ALK negative. Total dose of treatment was prescribed at 80% isodose and risk-adapted treatment schedules were used. All patients were treated with a minimum BED of 100 Gy.

Results

142 patients were included in the analysis with a median follow-up of 22 months. Patient characteristics and molecular biology determinations are listed in Table 1. Median progression free survival was 49 months. Stage ($p = 0.008$) and molecular biology factors (KRAS $p = 0.007$, unfavorable $p = 0.004$ and very unfavorable $p < 0.001$) were statistically significant with univariate analysis. Stage ($p = 0.02$) and the very unfavorable group ($p < 0.001$) were confirmed at the multivariate analysis. Median cancer specific survival was 73.7 months. Stage ($p = 0.02$) and molecular biology factors (KRAS $p = 0.009$, unfavorable $p = 0.025$, very unfavorable $p = 0.027$) were statistically significant in the univariate analysis as clinical predictors. Stage ($p = 0.03$) and the unfavorable group ($p = 0.06$) were confirmed in multivariate analysis. Local control at 12, 24 and 36 months was 95.8%, 83.6%, 80.1%, respectively. Stage ($p = 0.005$) and the very unfavorable group ($p = 0.001$) proved to be predictive for univariate analysis. Both factors were confirmed in

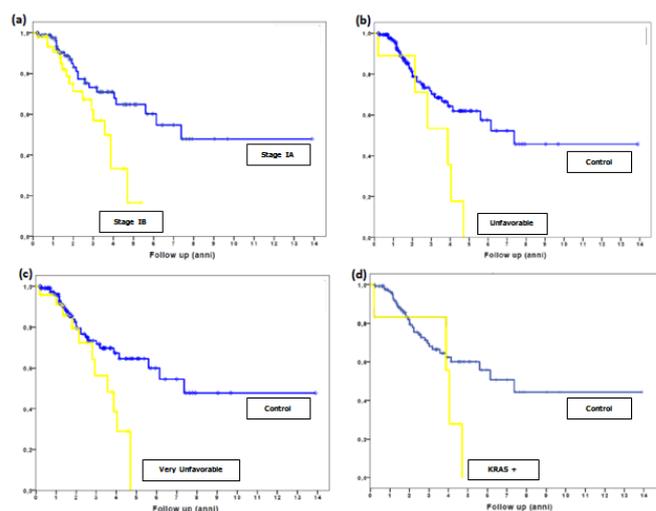
multivariate analysis (p respectively of 0.01 and 0.008). Systemic control at 12, 24 and 36 months was 90.1%, 72.5% and 67.7%, respectively. Stage (p < 0.001), histology (p = 0.04) and molecular biology factors (KRAS p < 0.001, unfavorable p < 0.001 and very unfavorable p < 0.001) proved to be predictive for univariate analysis. Only stage and the very unfavorable group were confirmed at the multivariate analysis (p of 0.03 and 0.002, respectively).

Conclusions

Molecular biology and histological parameter, such as KRAS, could select a population of patients with more aggressive neoplastic phenotype. These patients may be deserving of greater personalization of therapy by dose intensification or integration with systemic therapies.

	Number (%)	Average (range)
Sex		
Male	114 (80,3)	
Female	28 (19,7)	
Age		75 (52 - 86)
Stage		
Ia	88 (62)	
Ib	50 (35)	
PTV Volume		46,6 (4 - 143)
Mean Lung Dose		11,9 (2,50 - 19,80)
BED		114,4 (100 - 151,2)
Diagnosis		
Adenocarcinoma	83 (58,4)	
Squamous Cell Carcinoma	42 (29,6)	
NSCLCNOS	14 (9,8)	
Others	3 (2,1)	
Pattern		
Papillary	6	
Acinary	8	
Lepidic	2	
Micropapillary	1	
Solid	0	
Mixed	3	
TTF1		
Undetermined	93 (65,5)	
Negative	15 (10,5)	
Positive	34 (24)	
P40		
Undetermined	108 (76)	
Negative	13 (9,5)	
Positive	21 (14,5)	
KRAS		
Undetermined	136 (95,8)	
Mutated	6 (4,2)	
WT	0 (0)	
EGFR		
Undetermined	116 (81,7)	
Mutated	23 (16,2)	
WT	3 (2,1)	
ALK		
Undetermined	126 (88,7)	
Traslocated	15 (10,5)	
WT	1 (0,7)	
ROS1		
Undetermined	140 (98,6)	
Mutated	0 (0)	
WT	2 (1,4)	
B-RAF		
Undetermined	141 (99,3)	
Mutated	1 (0,7)	
WT	0 (0)	

Cancer Specific Survival



References:

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ABSTRACT FISICI

Predicting tumour motion during the whole radiotherapy treatment: a systematic approach based on real time MR

D. Cusumano^{1,2}, J.Dhont^{3,4,5}, L.Boldrini¹, G.Chiloiro¹, S.Teodoli⁶, M.Massaccesi⁶, B. Fionda⁶, F.Cellini⁶, L. Azario², J.Vandemeulebroucke^{4,5}, M. De Spirito², V. Valentini¹, D. Verellen^{3,7}

¹ *Dipartimento di Diagnostica per Immagini, Radioterapia Oncologica ed Ematologia, Istituto di Radiologia, Fondazione Policlinico A. Gemelli IRCCS, Roma – Italia*

² *Dipartimento di Diagnostica per Immagini, Radioterapia Oncologica ed Ematologia, Istituto di Fisica, Fondazione Policlinico A. Gemelli IRCCS, Roma – Italia*

³ *Faculty of Medicine and Pharmacy, Vrije Universiteit Brussel, Brussels, Belgium*

⁴ *Vrije Universiteit Brussel (VUB), Department of Electronics and Informatics (ETRO), Pleinlaan 2, B-1050 Brussels, Belgium*

⁵ *imec, Kapeldreef 75, B-3001 Leuven, Belgium*

⁶ *Dipartimento di Diagnostica per Immagini, Radioterapia Oncologica ed Ematologia, Fondazione Policlinico Universitario A. Gemelli IRCCS, Roma - Italia*

⁷ *Department of Radiotherapy, GZA Ziekenhuizen – Sint Augustinus, Iridium Kankernetwerk, Antwerp, Belgium*

Introduction and Aim

With the introduction of on-board magnetic resonance (MR) imaging, non-invasive continuous and direct monitoring of targets and organs at risk during the entire course of radiotherapy treatment (RT) has become available. Aim of this study was to analyse the respiratory-induced tumour motion and its variability of abdominal and thoracic lesions during the whole MR-guided RT treatment and to investigate the ability of 4DCT and 30 seconds free breathing cine-MR (30sMR) in predicting these quantities.

Materials and Methods

7 thoracic and 13 abdominal lesions were studied. During the simulation, a 4DCT and a 30sMR on a sagittal plan were acquired. All patients were treated by MR-guided RT adopting a free-breathing gating strategy, whereby the entire treatment is continuously monitored using the same MR acquisition adopted in simulation. The mean tumour motion amplitude ± 1 standard deviation (SD) was calculated in cranio-caudal (CC) and anterior-posterior (AP) direction for each MR-guided RT fraction. The mean motion amplitude on the full treatment (A_{treat}) was calculated as the mean of all

mean amplitudes calculated per fraction. Intrafraction amplitude variability (ΔA_{intra}) was defined as the mean of all amplitude SDs calculated per fraction. Interfraction amplitude variability (ΔA_{inter}) was defined as the standard deviation of A_{treat} . The tumour motion amplitude was also estimated by 30sec MR ($A_{30\text{s}}$) and 4DCT ($A_{4\text{DCT}}$) and these quantities were then compared with A_{treat} . The statistical significance of the difference between $A_{30\text{sMR}}$, $A_{4\text{DCT}}$ and A_{treat} was evaluated in terms of Wilcoxon Mann Whitney test. In order to evaluate the ability of 4DCT and 30sec MR in predicting interfraction and intrafraction motion variability, Spearmans correlation (SC) analysis was calculated between $\Delta A_{\text{intra}}-A_{30\text{sMR}}$ and $\Delta A_{\text{intra}}-A_{4\text{DCT}}$, as well as between $\Delta A_{\text{inter}}-A_{30\text{sMR}}$ and $\Delta A_{\text{inter}}-A_{4\text{DCT}}$.

Results

Differences between A_{treat} and 4DCT or 30sMR amplitude were not statistically significant, but 30sMR results to be more accurate than 4DCT in estimating A_{treat} (Fig.1)

The intra-fraction motion analysis showed that ΔA_{intra} was ≤ 4 mm in CC and ≤ 2 mm in AP for all patients. A strong correlation was observed between ΔA_{intra} and $A_{30\text{sMR}}$ (SC, CC: $r=0.77$, $p<0.001$, AP: $r=0.64$, $p<0.005$). Correlation between $A_{4\text{DCT}}$ and ΔA_{intra} was present only in AP direction (SC, CC: $r=0.43$, $p>0.05$, AP: $r=0.62$, $p<0.005$).The interfraction amplitude variability (ΔA_{inter}) observed

during treatment was ≤ 3 mm in CC and ≤ 1 mm in AP for all patients.The only parameter correlated to ΔA_{inter} was $A_{30\text{sMR}}$ in the CC direction (SC, CC: $r=0.63$, $p<0.005$, AP: $r=0.08$, $p>0.05$). Fig.2 shows all correlations in CC.

Conclusions

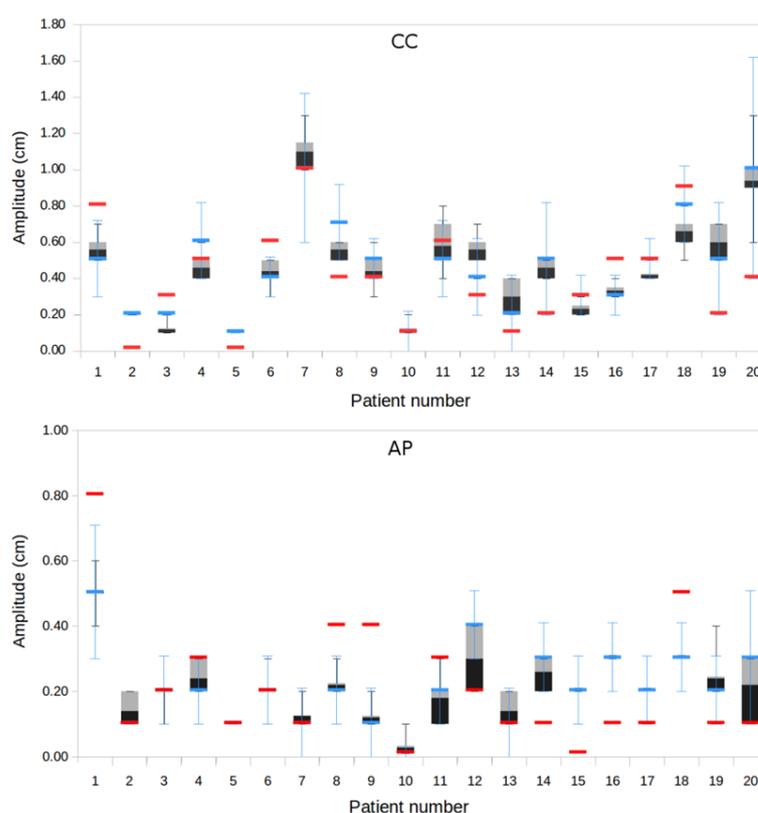


Figure 1: Boxplot representation of the tumour motion amplitude observed over the whole RT treatment, compared to the motion amplitude extracted from 4DCT (red bar), and the mean motion amplitude extracted from 30 s cine-MR (blue bar), per patient, in the craniocaudal (CC) and anteroposterior (AP) direction

The advantages observed with 30s cine-MR may be attributed to its higher soft-tissue contrast and time-resolved characteristics compared to 4DCT.

Lesions moving with small amplitude show limited amplitude variability throughout treatment, making passive motion management strategies seem adequate.

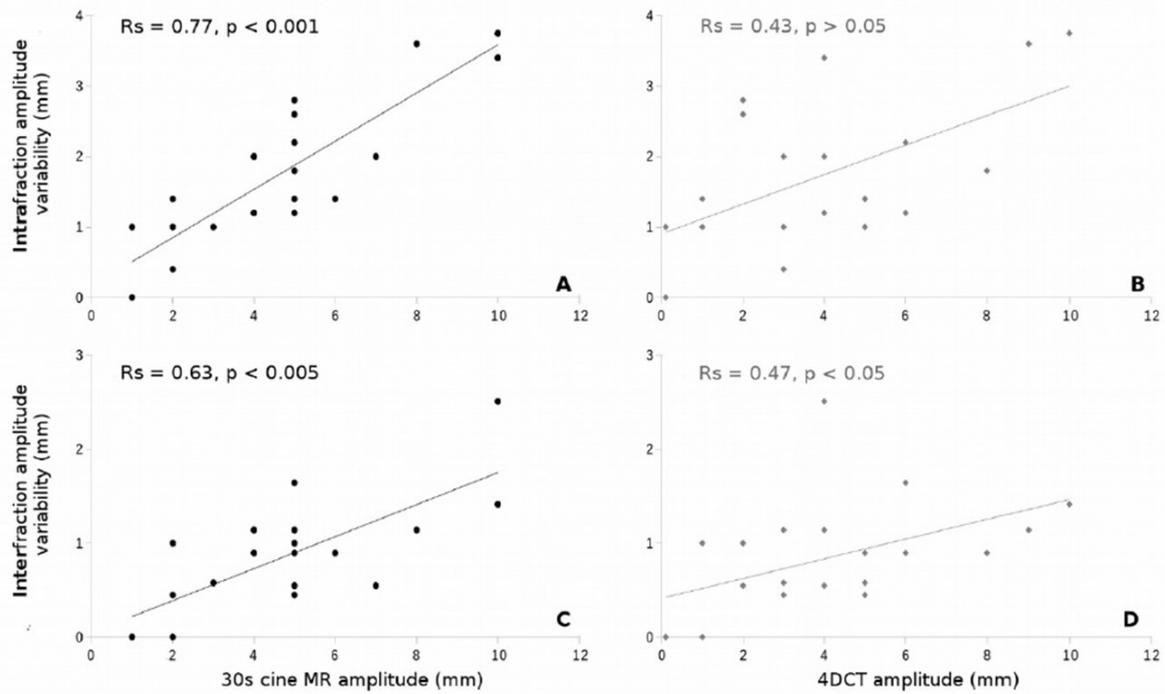


Figure 2: Correlation analysis between tumour motion amplitude calculated by 30 s cine-MR and the intra- (A) and interfraction (C) amplitude variability, and between the motion amplitude extracted from 4DCT and the intra- (B) and interfraction (D) amplitude variability.

Whole SBRT\SRS chain validation by End to End Test: a single institution experience

A.Ciarmatori¹, E.Argazzi¹, E.Belligotti¹, S.Giancaterino¹, M.Mariselli¹, F.Palleri¹, C.Biasi¹, F.Maurizi¹, M.Mazza¹, F.Bunkheila¹, M.Bono^{1, [L], [SEP]}

¹ *Azienda Ospedaliera Ospedali Riuniti Marche Nord, Pesaro*

Introduction and Aim

It is estimated that about 40% of adverse event in radiotherapy are related to implementation and commissioning process¹. Given that very high dose fractions of radiation are delivered in Stereotactic Body Radiation Therapy (SBRT) and Stereotactic Radiosurgery (SRS) the consequences of these events could be very dangerous and therefore the commissioning and implementation process require special attention and diligence. End to end test are a very useful tool to validate the whole SBRT\SRS chain to ensure quality and safety in the delivery process².

Materials and Methods

Two anthropomorphic phantoms (one Head&Neck, and one Dynamic Thorax Phantom) have been utilized to test immobilization, Computed Tomography (CT) simulation, 4DCT Motion Management, Contouring, Image fusion, Planning, Heterogeneity Calculation, Data Transfer, Quality Assurance, Image guidance, 4DCBCT, 6 degree of freedom set up and Dose Delivery. “Single isocenter – single target” and “single isocenter - multiple target” plans have been created using flattened filter (FF) and flattening filter free (FFF) beams. QA test have been performed with a high resolution 2D array of liquid filled ionization chamber and dose measurements have been carried out with micro-ionization chamber. Finally, small error (1-2 mm and 1-2°) have been simulated to test their dosimetric impact.

Results

Difference between planned and calculated doses were always less than 1.5% both in “single isocenter – single target” and “single isocenter – multiple target” plan. 4DCT and 4DCBCT provided consistent result and contouring defined on 4DCT safely included 4DCBCT based target. Magnetic Resonance Imaging (MRI) and CT image fusion provided very good agreement based on Dice index and Hausdorff distance measurements. FFF beams allow significant ($p<0.05$) beam time sparing without affecting dosimetric distribution. Small error in patient setup resulted in unneglectable (till 10%) dose difference.

Conclusions

Modern technologies allow to achieve sub-millimetre accuracy and very good dose agreement. However special attention should be used in all the steps of SBRT\SRS chain to optimize safety and quality of RT treatment.

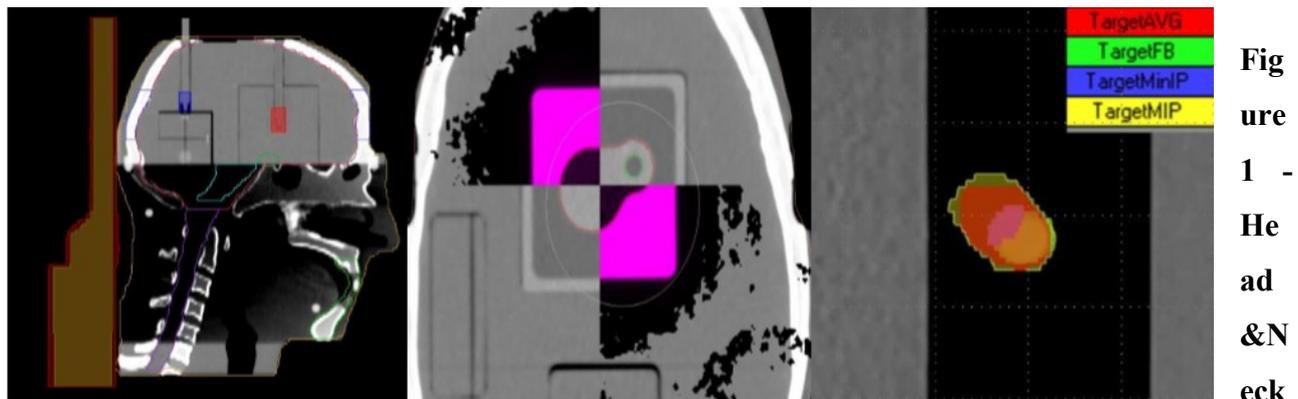


Figure 1 - Head & Neck

antropomorphic phantom with 2 ionization chamber (Left), MRI - CT image fusion Test (center), Impact of 4DCT on target defintion (right)

References:

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- [2] Solberg TD, Quality and safety considerations in stereotactic radiosurgery and stereotactic body radiation therapy: Executive summary., Pract Radiat Oncol. 2012 Jan-Mar;2(1):2-9.

Dosimetric evaluation of using bulk synthetic CT in MR-guided online adaptive radiotherapy

D.Cusumano¹, L.Placidi², S.Teodoli², L.Boldrini¹, F.Greco², S.Longo¹, F. Cellini², N. Dinapoli², V. Valentini¹, M. De Spirito¹, L. Azario¹

¹ *Fondazione Policlinico A. Gemelli IRCCS - Università Cattolica Sacro Cuore, Dipartimento di Scienze Radiologiche, Radioterapiche ed Ematologiche, Istituto di Radiologia, Roma – Italia*

² *Fondazione Policlinico Universitario A. Gemelli IRCCS, Dipartimento di Scienze Radiologiche, Radioterapiche ed Ematologiche, Roma – Italia*

Introduction and Aim

The online MR-guided adaptive Radiotherapy (MRgART) workflow relies on the assignation of the water relative electron density (RED) map to the daily MR image (dMRI), in order to allow the dose calculation [1].

One promising approach to overcome the inter-fraction RED map variability consists in daily generating a synthetic CT (sCT) by segmenting the dMRI in 5 density levels (air, lung, fat, tissue and bone) and assigning a RED bulk value to each level according to ICRU 46 recommendations [2].

Aim of this study is to evaluate the dosimetric accuracy of such approach in the case of abdomen and pelvis districts. The dosimetric results will be compared to those obtained by using a tailored sCT, generated by assigning for each patient its median bulk RED values.

Materials and Methods

26 patients were initially enrolled in the pelvic and abdomen district.

For each patient, a planning CT (pCT) was acquired and segmented in the 5 density levels, then median RED (mRED) values were calculated for fat, soft tissue and bone.

Correlation between mREDs and clinical parameters (age, sex, body mass index) was investigated by using the Pearson Correlation Coefficient (PCC).

This investigation was repeated on an extended dataset (30 female) to further investigate correlation between bone and age in women.

In order to assess the dosimetric accuracy of using sCT, two sCTs were generated by assigning RED bulk values to the segmented levels on pCT: the sCT_{ICRU} uses the RED values recommended by ICRU 46, the sCT_{tailor} uses the median patient-specific RED values.

The same treatment plan was calculated on the sCTs and compared to those calculated on pCT in terms of 1%/1mm gamma analysis and dose volume histogram (DVH) parameters.

For DVH analysis, V95%, D98% and D2% of the PTV and 3 parameters (mean dose, D1cc and D98%) related to the organ at risk (OAR) closest to the PTV were considered respectively.

The statistical significance of the difference between the two sCTs were evaluated using Wilcoxon Mann Withney

Results

The only significant correlation between mREDs and clinical parameters was observed between bone and age in women (PCC=-0.886 on the extended dataset, Figure 1).

For the dosimetric analysis, high agreement was found between dose calculated on sCTs and pCT: γ passing-rate was $91.2\% \pm 6.9\%$ for sCT_{ICRU} and $93.7\% \pm 5.3\%$ for sCT_{tailor}. A statistically significant gain in using sCT_{tailor} respect to sCT_{ICRU46} was found ($p = 0.0013$)

Figure 2 contains the box-plot analysis related to the difference of the DVH values respect to those calculated on pCT. The differences observed using sCT_{tailor} are closer to zero if compared to those calculated on sCT_{ICRU46}, also if no statistical significance was observed.

Conclusions

Bulk sCT is a reliable method to address the inter-fraction variability that influences the ED map. In particular, assigning patient specific RED values improves the dose calculation accuracy, guarantying higher reliability for MRgART

References

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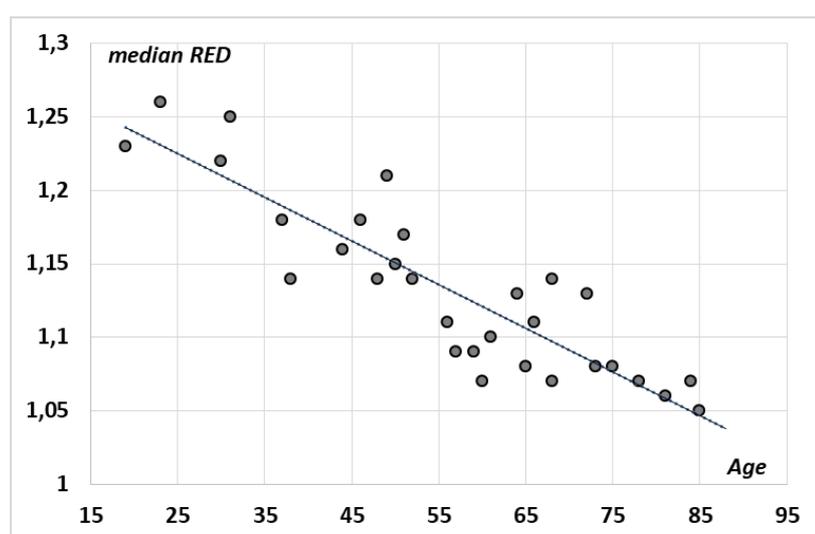


Figure 1 – Plot of the median

RED values of the bone density in women in function of the age

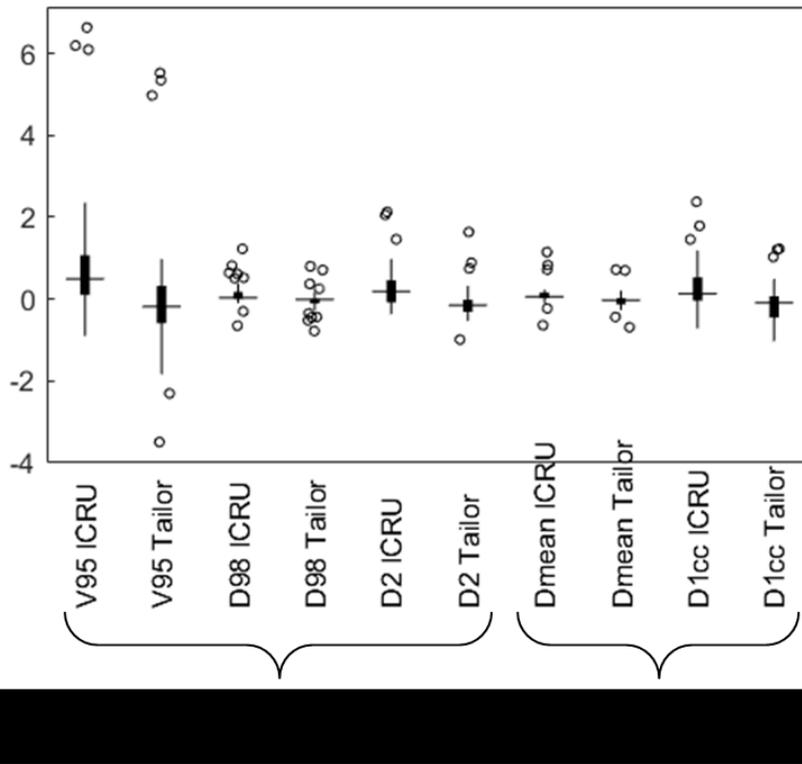


Figure 2 – Box-plot analysis of the differences of sCT_{tailor} and sCT_{ICRU46} respect to pCT for the DVH parameters related to PTV coverage (V95, D98, D2) and OAR sparing (D98, mean dose and D1cc)

Comparison of online 6D image registration of CBCT and in-room hybrid infrared X-Ray based monitoring system for SBRT

D. Aiello¹, G.R. Borzì², V. Umina², L. Marino², A.M. Di Grazia²

¹*Fondazione Istituto Oncologico del Mediterraneo (FIOM), Viagrande (CT)*

²*REM Radioterapia, Viagrande (CT)*

Introduction and Aim

The goal was to compare the residual setup errors measured with an in-room hybrid infrared X-Ray six degree-of-freedom (6D) monitoring system and kilovoltage cone-beam computed tomography (CBCT) in patients receiving stereotactic body radiotherapy (SBRT). The first device performs the pre-positioning using an infrared optical system based on body markers, and an X-Ray imaging system for target verification and adjustment using the internal anatomy. On the other hand, CBCT technology, through the acquisition of a patient's 3D image, allows for positioning control using both bone anatomy and soft tissue.

Materials and Methods

On a dedicated stereotactic linear accelerator, from January 2017 to July 2018, 93 patients with extracranial tumors were submitted to image-guided (IG)-SBRT for a total of 113 lesions and 343 treatment sessions. For 85 of these patients (311 treatment sessions) the 6D image registrations on infrared X-Ray monitoring system were performed together with CBCT. Planning techniques were dynamic conformal arc therapy or hybrid intensity-modulated radiotherapy with non-coplanar fields, or volumetric modulated arc therapy. All patients were initially located using personalized immobilization systems. Setup corrections were determined and corrected by means of registrations of X-Ray images with the corresponding digitally reconstructed radiographs using the 6D-fusion algorithm. At the end of each treatment session, with the couch at 0°, the residual setup error was determined by means of registrations of CBCT images with the planning CT using online 3D fusion; for each session, to analyze the residual setup errors displacements were evaluated.

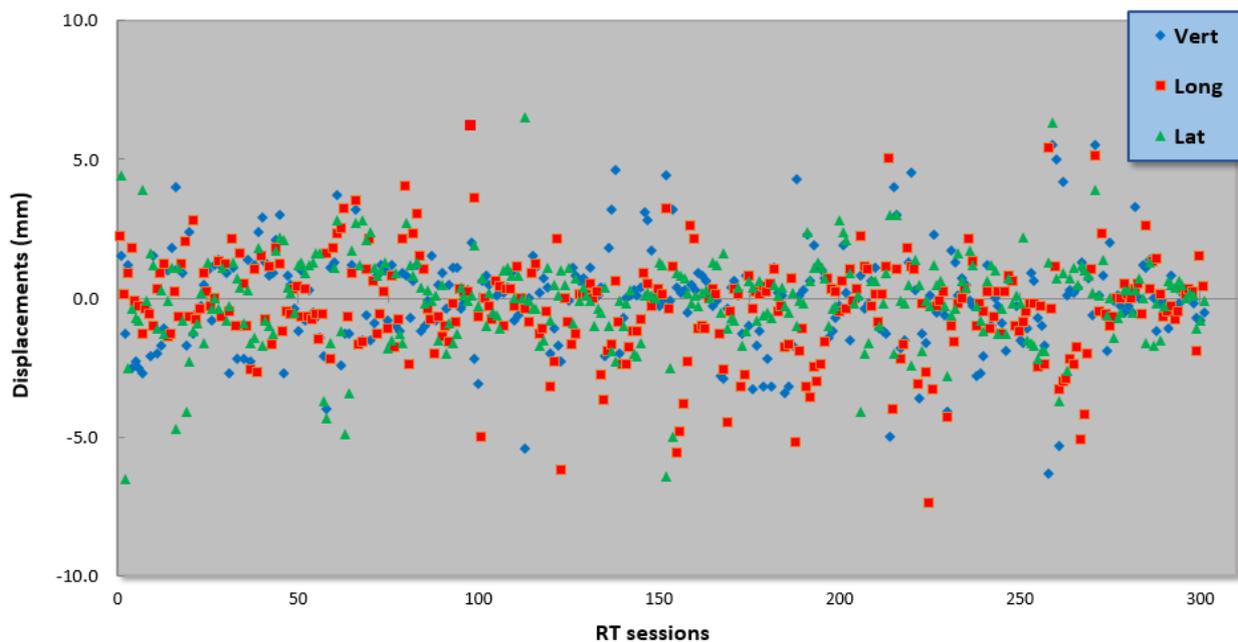
Results

The average residual error differences (absolute values) between CBCT and in-room hybrid infrared X-Ray based monitoring system image registrations were 1.28 ± 1.19 mm, 1.31 ± 1.28 mm and 1.14 ± 1.12 mm in the vertical, longitudinal and lateral directions, respectively.

Conclusions

Our study showed a good agreement on the setup accuracy and image registration between the hybrid in-room monitoring system and CBCT for patients receiving SBRT. The two IGRT systems presented similar precision. Nevertheless, in-room X-Ray based monitoring system offers additional

benefits in terms of capability to quantify all rotational errors, fastest automated positioning in 6D even for non-coplanar fields and smaller doses, representing a valid alternative to CBCT with complementary information in IG-SBRT.



Monitor Units constraints for SBRT plans and prostate cancer.

N. Cavalli¹, E. Bonanno¹, G. Stella², G. Pisasale¹, N. Ricottone¹, A. D'Agostino¹, A. Girlando¹, C. Marino^{1,2}

¹*HUMANITAS-Centro Catanese di Oncologia, Catania*

²*Scuola di Specializzazione di Fisica Medica, Università di Catania*

Introduction and Aim

The treatment of low-intermediate- risk prostate cancer with a highly hypofractionated five-fraction regimen is more and more employed because of tumor biology. Stereotactic Body Radiation Therapy (SBRT) VMAT plans are often characterized by strongly modulated radiation fields with continuous variations in complex multileaf collimator patterns, gantry speed and dose rate during delivery.

In this work the correlation between total monitor units (MUs) constraints, dosimetric findings and pre-treatment verifications has been studied for prostate SBRT VMAT plans.

Materials and methods

A retrospective analysis on 5 SBRT prostate treatments has been performed. Plans were been accomplished with Varian Eclipse treatment planning system (*version 13.6.23*) and optimization was performed using the Photon Optimizer (PO 13.6.23) on TrueBeam™ 2.5. The so called MU Objective tool implemented in RapidArc optimization engine was used. This tool allows setting the range and the relative priority to the minimum and maximum number of MU employed for a plan optimization. Dose prescription was 35 Gy in 5 fractions, using 10MV-FFF photon beams and plans were calculated using Acuros XB 13.6 algorithm. Plan objectives were set according with the AAPM TG 101. All plans were calculated with and without constraints on MUs. For each case the 2 plans were compared in terms of DVH objectives, MUs, modulation complexity coefficient (MU/Gy) and pre-treatment quality assurance performed with the EPID and Epiqa software, using 2%-1mm criteria for the Gamma Analysis.

Results

Average MUs were 973 and 1120 while modulation coefficient were 277.5 MU/Gy and 320 MU/Gy, respectively for plans with and without forced MUs. Differences in plans quality have been found in terms of DVH. In fact, for 3 of the 5 analyzed case,

Gamma Analysis Index (GAI) 2%-1mm

Case N°	Unforced MUs	Forced MUs
1	95.3 %	96.8 %
2	95.5 %	97.2 %
3	95.6 %	97.8 %
4	95.2 %	98.1 %
5	96.4 %	98.7 %

the use of “MU objective” involve a better PTV coverage and a reduced dose to OARs. Pre-treatments verifications showed a better agreement between calculated and delivered dose distribution for all SBRT plans obtained forcing MUs. The table shows pre-treatment quality assurance results. All plans were acceptable with a Gamma Analysis Index (GAI) > 95%.

Conclusions

Important discrepancies have been found in terms of total MUs and of modulation complexity coefficient, that are considerably reduced for plans obtained forcing the MUs.

SBRT plans obtained using forced MUs reveals an increasing of GAI value associated with MUs reduction.

In our opinion, for SBRT treatments further studies are necessities on a wider sample of cases to understand if minimizing modulation (i.e. decreasing total MUs) could be a good solution for all SBRT treatment plans.

SBRT for lung tumors: precise target definition and clinical workflow.

C.Gasperi¹, S. Borghesi², E.Tucci²_[SEP]

¹ Azienda USL Toscana sud est, Health Department Staff, Medical Physics Unit, San Donato Hospital, Arezzo

² Azienda USL Toscana sud est, Radiotherapy Unit, San Donato Hospital, Arezzo

Introduction and Aim

Stereotactic body radiotherapy (SBRT) for lung tumors, has gained an increasing importance, due to success attributable to the good clinical outcomes and represents an alternative in operable patients. Precise definition of the target volume is one of the crucial factors in the management of non-small cell lung cancer (NSCLC) with SBRT. It has widely recognized that the motion pattern of lung tumors varies greatly among patients. Therefore tumor motion should be assessed with patient specific image acquisition, to ensure adequate tumor coverage and minimizing dose to the Organ at Risk. The "gold standard" approach for defining an Internal target volume (ITV) [1] is using gross tumor volume (GTV) delineated over several phases in course of one respiratory cycle. It is a time consuming method and different Institution have adopted several alternative techniques which compress all temporal information into one CT image set, to optimize work flow efficiency. The purpose of this study is to evaluate alternative target segmentation strategies with respect to the gold standard.

Materials and Methods

Twenty lung cancer SBRT patients, treated on a linac with 4 mm width multileaf-collimator (MLC), were analysed retrospectively. From the acquisition of a low-pitch helical CT scan (Untag CT) combined with a respiratory monitor system signal, four-dimensional CT scans were reconstructed for each patient. ITV was delineated based on 4 single respiratory phases and on MaxIP, MinIP, MeanIP CTs and Untag CTs. Statistical analysis was performed using the Dice similarity coefficient (DSC). The relative position between the delineated target was evaluated calculating the centroid distance between volumes.

Results

GTVs derived from Untag, MaxIP and MeanIP image set are the least comparable with the single phase ITV delineation, with DSC = 0.936-0.551, DSC=0.877-0.331 and DSC=0.877-0.354 respectively. MinIP GTV delineation was less comparable to the 4DCT ITV with DSC=0.80-0.07. The differences in relative position of target volume localization were small and in all cases < 3mm. The mean differences \pm SD of the centroid distances for ITV and GTVUntag, GTVmaxIP,

GTV_{meanIP}, GTV_{minIP} were 0.18 ± 0.16 cm, 0.18 ± 0.16 cm, 0.23 ± 0.19 cm, 0.26 ± 0.19 cm respectively.

Conclusions

Our results indicate that the delineated targets are comparable for Untag, MaxIP and MeanIP CT with respect to the standard ITV from 4DCT single phase method. The use of the MinIP leads to an underestimation of the contoured volume. The spatial accuracy of the tumor volume is limited to a range within 3 mm (mean distance of the volume centroids) and this leads to a good spatial agreement between PTVs, if generated by expanding a uniformly isotropic 5 mm margin from ITV and GTVs. Among various techniques used for image segmentation, Untag, MaxIP and MeanIP GTVs could be considered as a geometrical surrogate of the standard ITV.

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Single Isocenter approach to multiple brain metastases using volumetric modulated radiosurgery

G.Pastore¹, C.Menichelli¹, A.Fanelli¹, E.Lombardo¹, F.Casamassima¹ [SEP]

¹ *Department of Radiation Oncology, Ecomedica, Empoli*

Introduction and Aim

Brain metastases are the most common intracranial tumors for patients with cancer. Primary treatment approaches are surgery and radiotherapy. Surgery involves rapid and reliable relief of neurological symptoms and establishment of local control, however, surgical resection is invasive and is usually limited to patients with a single lesion. Patients with multiple brain metastases are usually treated by WBRT. It offers effective palliation of neurological symptoms, but causes adverse effect on neurocognitive function and, frequently, shows relapses. SRS represents an effective treatment for patients with multiple brain metastases. The use of different treatment plans for different metastases raises the problem of the overall distribution of low doses outside the target, which are less easily controllable. This study is aimed to verify the possibility of using a single VMAT plan with a single isocenter to multiple brain metastases.

Materials and methods

45 patients with multiple brain metastases (range 2-7) were selected. Anatomical contours and targets were delineated on the fused contrast-enhanced CT and magnetic resonance image sets. The brain metastases prescription dose was 18 Gy to 70% isodose in a single fraction. VMAT treatment plans were generated with 4 non coplanar arcs using TPS based on X-ray Voxel Monte Carlo (XVMC) and constraint optimization algorithms with biological cost functions. A photon energy of 6 MV was employed throughout this study. The dose calculation grid size and the calculated dose statistics were set to 2 mm and 0.5% (normalized standard deviation) per plan, respectively. Quantitative and dosimetric evaluation of the plans was performed using the DVH. Conformity index (CI) and gradient index (GI) were calculated. The number of MU was also recorded. To verify the VMAT plans gamma analyses under 3%/3 mm and 2%/2 mm criteria, with global percent differences, were used. Local Control (LC) was also examined to verify the treatment effectiveness.

Results

The mean CI was 0.7, but CI decreased to 0.28 when there was a short distance between two targets (<1 cm). The mean GI was 12, but again decreased if the distance between two targets was lower than 1cm. The mean healthy brain dose was 3.85±0.59 Gy and V12= 10.88cc. The mean treatment delivery time was 23.6 min. The mean gamma passing rates under each of the 3%/3 mm and 2%/2 mm criteria were 98.5% (range 99.1–96.5%) and 88.8% (range, 90.1–87.4%), respectively. LC at 3

and 6 months was 97.2% and 89.8% respectively, considering that primary tumor was lung in 46% of pts, breast in 20.2%, melanoma in 17% and other in 16,8%.

Conclusions

VMAT technique appears useful to reach eradicated doses to metastases controlling the distribution of the low doses outside the target with a single isocentre. These useful dose distributions permit to offer a good solution for patients with limited number of brain metastases not amenable to surgery. But this technique involves long time of treatment.

Retrospective clinical evaluation of 4D motion effects in the robotic radiosurgery treatment of lung cancer

S. Trivellato^{1,2}, E. Rondi¹, S. Vigorito¹, E. Miglietta³, G. Piperno³, A. Ferrari³, B. A. Jereczek-Fossa^{3,4}, F. Cattani^{1,†,§}

¹*Unit of Medical Physics, European Institute of Oncology, Milan, Italy*

²*Department of Physics, University of Milan, Milan, Italy*

³*Division of Radiation Oncology, European Institute of Oncology, Milan, Italy*

⁴*Department of Oncology and Hemato-oncology, University of Milan, Milan, Italy*

Introduction and Aim

Stereotactic body radiation therapy (SBRT) has emerged as a non-invasive standard treatment modality for early stage lung cancer [1-3]. Respiratory management is mandatory to secure SBRT dose conformity and it should be individually assessed [4]. An available treatment planning system for a robotic radiosurgery system is now offering the 4D treatment planning and optimization feature to take into account tissue motion recorded in a 4D computed tomography (4D-CT) [5]. The aim of the study is to exploit this 4D module for a retrospective clinical analysis of 4D motion effects on target coverage and organs at risk (OARs) sparing during robotic radiosurgery in lung cancer treatment.

Materials and methods

Ten consecutive lung cancer patients, 5 in upper and 5 in lower lobe, have been retrospectively selected. The robotic system allows treating lesions that cannot be fully tracked. In this so-called 0-view modality, the internal target volume is defined in the 4D-CT as the envelope of the lesion volume in the full-exhale and full-inhale CT series. A set-up margin of 5 mm is added to account for estimated errors of the 4D procedure to get the planning target volume (PTV). The conventional 3D module optimizes and calculates dose distributions on the reference full-inhale phase. The 4D module uses b-splines deformable image registration to accumulate dose distributions calculated on each static 3D-CT image of the 4D-CT dataset. The final 4D dose distribution is shown on the selected reference image. For each patient, 3D optimization was performed and followed by both 3D and 4D calculations (3Dopt+calc Plan and 3Dopt4Dcalc Plan). A complete 4D optimization and calculation (4Dopt+calc Plan) have been performed when the 3Dopt4Dcalc Plan resulted clinically suboptimal. All dose distributions were obtained using the ray-tracing algorithm and 8 respiratory phases.

Results

The measured range of lesion displacement was 0-6 mm and 4-19 mm for upper and lower lobe, respectively. Plans have been prescribed at the 80% isodose. 3Dopt+calc Plans showed a median volume covered by the 100% isodose (V100%) of 98.2% with a median minimum dose (Dmin) of 93.5%. 3Dopt4Dcalc Plans resulted in a median V100% of 95.6% and a Dmin of 87.5%. Variations in V100% metric are in the range (-14.9%, 0%). Seven out of 10 patients have been reoptimized with the 4D Module, all lower lesions and 2 upper lesions. 4Dopt+calc Plans showed a median V100% of 97.3% with a median Dmin of 93.8%. Among OARs, most relevant variations have been registered in the heart maximum dose. Details are shown in Table 1 and 2.

Conclusions

Due to recorded variations, 70% of plans have been re-optimised. The 4D module is a powerful tool to manage organ motion when lesion tracking is not possible, especially for lesions in lower lobes or close to moving OARs. Further studies will increase the number of patients and validate results with film measurements in a 4D anthropomorphic phantom.

Table 1 Dosimetric results for total population, upper and lower lobe lesions: comparison between 3Dopt+calc, 3Dopt4Dcalc and 4Dopt+calc Plans.

		Total (10 patients)					
		3Dopt+calc		3Dopt4Dcalc		4Dopt+calc	
D _{min} [%]		93.5		87.5		93.8	
		(85.1 - 96.7)		(74.6 - 96.1)		(85.6 - 95.5)	
V _{100%} [%]		98.2		95.6		97.3	
		(95.2 - 98.8)		(83.3 - 98.3)		(96.0 - 98.7)	
		Lower lobe (5 patients)			Upper lobe (5 patients)		
		3Dopt+calc	3Dopt4Dcalc	4Dopt+calc	3Dopt+calc	3Dopt4Dcalc	4Dopt+calc
D _{min} [%]		94.2	86.1	93.8	92.8	88.9	89.8
		(91.0 - 95.8)	(74.6 - 93.4)	(92.1 - 95.5)	(85.1 - 96.7)	(81.6 - 96.1)	(85.6 - 93.9)
V _{100%} [%]		98.2	90.1	97.3	98.4	97.0	97.1
		(95.2 - 98.6)	(83.3 - 96.8)	(96.0 - 98.7)	(97.0 - 98.3)	(92.1 - 98.2)	(96.8 - 97.4)
Displacement [mm]		2.3 (0.0 - 5.9)			11.3 (4.0 - 18.7)		

Values are presented as median (min-max).

3Dopt+calc: dose distribution of 3D optimized and calculated plans; 3Dopt4Dcalc: dose distribution of 3D optimized and 4D calculated plans; 4Dopt+calc: dose distribution of 4D optimized and calculated plans; D_{min}: minimum target dose; V_{100%}: percentage volume covered by the 100% isodose.

Table 2 Variation between 3Dopt+calc and 3Dopt4Dcalc dose distributions for main organs at risk (OARs).

OARs, D _{max}	Δ%
Spinal cord	-0.2 (-4.1 - 1.5)
Oesophagus	-0.5 (-4.9 - 2.1)
Heart	-3.0 (-17.5 - 1.9)
Trachea	-0.2 (-2.0 - 5.7)

Values are presented as median (min-max).

Δ%: percentage deviation of 3Dopt4Dcalc maximum doses with respect to 3Dopt+calc maximum doses.

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A crowd-knowledge-based analysis of DVHs in SBRT: first steps towards a national virtual audit

A. Savini¹, M. Fusella¹, M. Esposito¹, V. Ardu¹, G. Benecchi¹, A. Bergantin¹, G.R. Borzi¹, S. Bresciani¹, E. Cagni¹, C. Carbonini¹, M. Casati¹, S. Clemente¹, R. Consorti¹, S. Cora¹, E. DeMartin¹, R. ElGawhary¹, M.D. Falco¹, D. Fedele¹, C. Fiandra¹, M.C. Frassanito¹, C. Garibaldi¹, G. Gasperi¹, F.R. Giglioli¹, G. Guidi¹, I. Ielo¹, V. Landoni¹, S. Magi¹, T. Malatesta¹, C. Marino¹, L. Masi¹, E. Moretti¹, S. Naccarato¹, B. Nardiello¹, R. Nigro¹, G. Pastore¹, M. Presello¹, V. Ravaglia¹, S. Russo¹, L. Strigari¹, S. Strolin¹, C. Talamonti¹, A. Vaiano¹, S. Vigorito¹, E. Villaggi¹, M. Stasi¹, P. Mancosu¹

¹ *SBRT Working Group, AIFM - Italian Association of Medical Physics, Italy*

Introduction and Aim

Currently, most of the multicenter analyses on treatment planning rely on the extraction of selected data from the DVH of each plan. A grouped analysis can be biased due to different algorithms implemented in different TPSs used to generate the DVH. In this work we used a consistent method to present a preliminary analysis of multiple data coming from a national survey on stereotactic body radiotherapy (SBRT) planning.

Materials and Methods

A single spine case was shared among 36 radiation oncology centers. The dose prescription was 30 Gy in 3 fractions with specific constraints on target coverage and dose to nearby organs at risk. Data were collected in DICOM-RT format. A script was developed in R language using the RadOnc R-Package for recalculating the DVHs using the same algorithm. Specific DVH points (V30Gy, D90%, D2%) collected from the centers were compared with those recalculated with RadOnc. A grouped analysis of recalculated DVHs was performed therefore eliminating the bias due to different DVH calculation algorithms.

Results

Differences between collected and recalculated DVHs were minimal, however in some cases deviations up to 1.5% were observed. The multiple-DVH analysis showed a notable variability on target dose level (Fig.1), up to 150% likely related to constraints on target coverage and SBRT technique. This variability was caused mainly by different planning optimization strategies, rather than by the use of a specific treatment technology.

Conclusions

The observed variability suggests that comparable standards in patient treatment among different centers can be obtained if a consistent high-level data sharing capability is granted. In the strive to

harmonize the planning process, this analysis constitutes a first step toward the creation of a platform of crowd-knowledge-based planning guidelines. This platform could represent a high-quality benchmark for those centers that are willing to implement SBRT techniques (concept expressed in Fig.1).

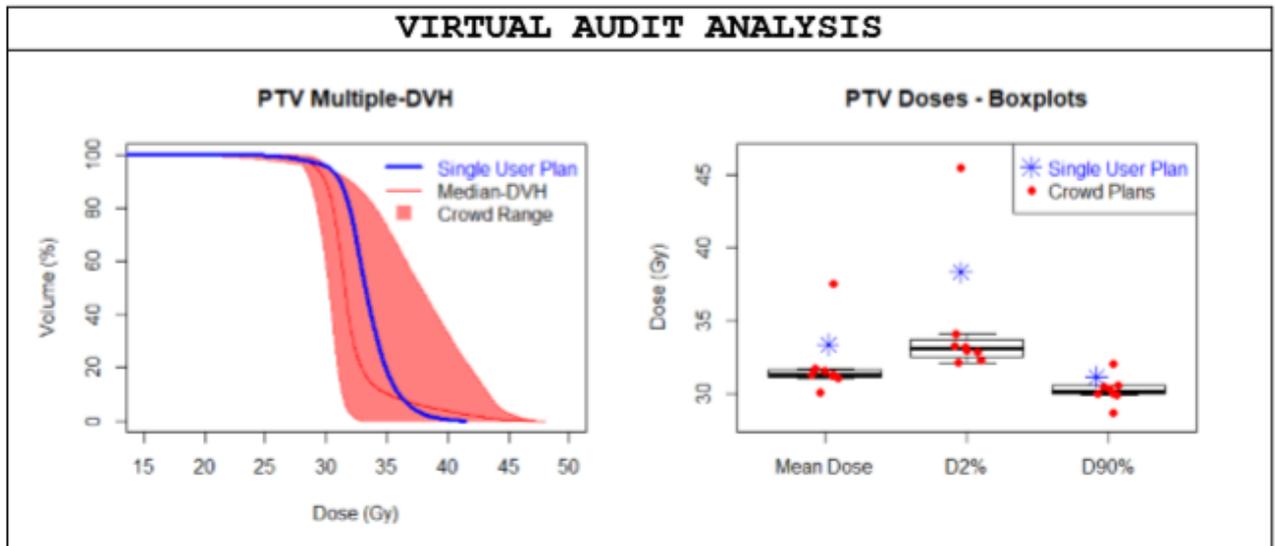


Figure 1

VMAT patient-specific QA for SBRT treatments through Gafchromic™ EBT3 film dosimetry and FILM-QA software^[1]

G. Stella^{1,2}, N. Cavalli¹, E. Bonanno¹, A.M. Gueli², A. Girlando¹, C. Marino^{1,2}^[1]

¹ *Humanitas Centro Catanese di Oncologia – Catania*

² *Specialty School in Medical Physics, University of Catania.*

Introduction and Aim

In order to optimize the procedures for VMAT patient-specific quality assurance for SBRT treatments, plans were verified with dose map measurements by Gafchromic™ EBT3 film dosimetry and FILM QA software. In the last year, a new protocol for measurement of patient or application films was developed. It combines the digitization of the application film with the digitization of two calibration or reference films from the same production lot as the application film [1]. The aim of this work is to provide indications on the choice of reference dose value.

Materials and Methods

6FFF and 10FFF photon beams were used to obtain calibration dose curves from 0 to 25 Gy and to study energy dependence of Gafchromic™ EBT3. Films were digitized with Epson 10000 XL and analyzed with FILM QA software. Triple-channel method was used to improve film dosimetry accuracy [2]. 10 SBRT-VMAT treatment plans, calculated with Eclipse™ TPS and delivered with TrueBeam 2.5, were imported as DICOM files in FILM QA software. These files contain all plan data including dose range and isocenter coordinates. To eliminate scan-to-scan variability and uncertainty therefrom, EBT3 films, exposed to each VMAT arc, were digitalized in a single scan with two reference films: one film exposed to a known dose and one unexposed film. The choice of the known reference dose value was made following two different methods: (a) for each calculated arc the density dose distribution was obtained and the dose value related to maximum frequency was chosen as reference; (b) 80% of the maximum dose value of each calculated plane was used as reference [3]. Pre-treatment verifications in terms of gamma analysis approach (3%/3mm and 2%2mm criteria and 95% passing rate) were performed. To investigate the statistical discrepancies between global gamma index obtained with the two different methods, Student T-tests was used.

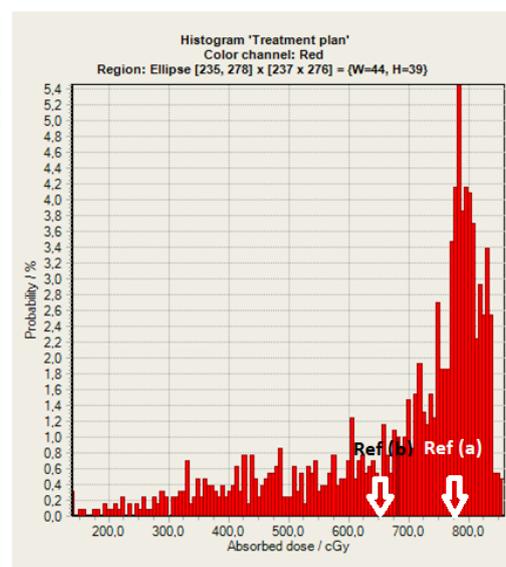
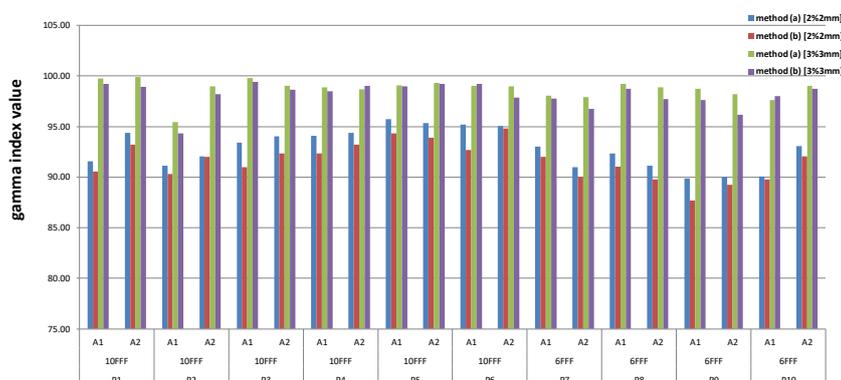
Results

The average passing rate for 2%2mm criteria was 92.84% for method (a) and 91.61% for method (b). P-value calculated by t-test was $0.022 < 0.050$ (threshold significance level) and it suggests that the observed data is sufficiently inconsistent with the null hypothesis. With a significance level of 95% the two data set obtained with different methods are statistically distinguished. The average passing rate for 3%3mm criteria was 98.72% for method (a) and 98.14% for method (b). P-value

calculated by t-test was $0.055 < 0.100$ (threshold significance level) and it suggests that the observed data is sufficiently inconsistent with the null hypothesis with a significance level of 90%.

Conclusions

This approach allowed to establish a single criterion of choice for reference know dose value to eliminate scan-to-scan variability and uncertainty therefrom. Under particular experimental conditions, the use of EBT3 film dosimetry analyzed with FILM QA software shows to be an accurate QA method for VMAT-SBRT treatment plans.



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SBRT for prostate cancer: preliminary results from a three fraction schedule

V. Landoni¹, A. Farneti², G. Iaccarino¹, A. Soriani¹, A. Faiella², B. Saracino², M. G. Petrongari², F. Spasiano² and G. Sanguineti²

¹ *Medical Physics Dept, IRCCS - Regina Elena National Cancer Institute, Rome, Italy*

² *Radiotherapy, IRCCS - Regina Elena National Cancer Institute, Rome, Italy*

Introduction and Aim

Hypo-fractionation for prostate cancer has shown to be a successful strategy due to the low value of the alfa/beta ratio for this tumor. Furthermore, precision in delivery has allowed to increase the therapeutic ratio and safely administer stereotactic body radiation therapy in five fractions. Our aim is to investigate the possibility of an ablative treatment in three fractions escalating the dose to the prostate while respecting the tolerance of normal tissues.

Materials and methods

Since November 2015, 19 patients have been enrolled in a phase I-II feasibility trial. All patients had low (11 pts) or intermediate/favourable risk (8 pt) disease. Dose prescription was tentatively set at 40 Gy in three fractions, while limiting the dose to 1cc of rectum, bladder (without trigone), trigone to 30Gy, 38Gy and 30Gy respectively and to 0.1cc of urethra to 30Gy. These dose volume objectives on OAR yielded over PTV coverage. Patients were specifically prepared with gold fiducials inserted in the prostate gland and with a gel spacer to dislocate rectum. A simulation CT and MRI were acquired with the patient immobilized and with urethral catheter. Rectal and bladder filling were controlled also at each treatment. Fifteen patients received a LINAC based treatment while 4 were treated with CK. Patients underwent a CBCT imaging before and after the delivery of each arc, while at Cyberknife the imaging frame consisted of the acquisition of 1 image per minute. Pre-treatment dosimetric verification was performed for each patient.

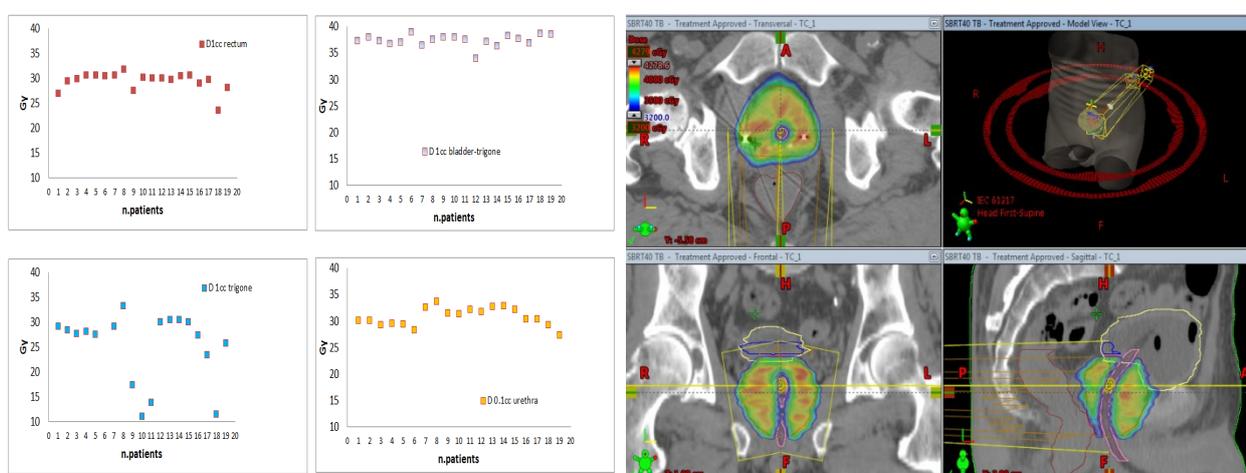
Results

Median clinical target volume, i.e. prostate gland, (CTV) was 52.3cc (range 23.3-92) while median planning target volume (PTV) was 90.7cc (range 48.2-140.7). Mean D95% at PTV was 34.4Gy (SD 1.6Gy). Mean percentage volume receiving 38Gy was 70.7% (SD 12.4%) and 64.3% (SD 12.2%) for CTV and PTV respectively. In any case maximum doses were always inside the PTV and below 44Gy, 110 % of the prescription dose. Mean doses to 1cc of organs at risk were kept below 27.5Gy (SD 1.2Gy) for the rectum, 37.9Gy (SD 1.3Gy) for the bladder (without trigone) and 21.9Gy (SD 9.3Gy) for the trigone. No more than 29.3Gy (SD 1.6Gy) were given to 0.1cc of urethra. 12 patients reached a follow up of 3 months median 8.5, range 3.6-32.5. One patient developed grade 2 acute

GU toxicity and 1 patient grade 2 acute GI toxicity. No grade 3 or more acute reactions were observed. No late grade 2+ toxicity has been reported so far.

Conclusions

Due to the difficulty to obtain highly dis-homogeneous dose distributions to keep the dose to organs at risk below the dose volume limits established in the protocol, the intended prescription was actually limited to a coverage of 34.4 Gy (range 30 Gy-36 Gy) to the 95 % of the PTV. On the other hand, these preliminary data show that acute toxicity is mild, suggesting that relaxation of dose constraints on OAR (and thus better PTV coverage) can be pursued.



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Normal lung tissue complications in MR-Linac radiotherapy

S.Gholami¹, F. Longo², S. Shahzadeh³, H.A Nedaie¹, R. Sharp⁴, and A. S.Meigooni⁵

¹ *Cancer institute, Tehran University of Medical Sciences, Tehran, Iran*

² *Department of Physics, University of Trieste and INFN Trieste, Italy*

³ *Department of Medical Radiation Engineering, Shahid Beheshti University, Tehran, Iran*

⁴ *Department of Health Physics and Diagnostic Sciences, University of Nevada, Las Vegas, Nevada, United States*

⁵ *Comprehensive Cancer Centers of Nevada, Las Vegas, Nevada, United States;*

Introduction and Aim

To investigate normal lung tissue complications in both magnetic resonance (MR) images based linac and conventional radiotherapy (RT) techniques using Monte Carlo (MC) simulation methods and a 4D-XCAT digital phantom.

Materials and Methods

The Geant4 toolkit (Version 10.1.p02) was used to simulate a 6 MV photon beam from a Varian2100C linear accelerator. For MR-linac evaluations, a homogenous magnetic field of 1.5 Tesla was applied in both perpendicular and parallel directions relative to the radiation beam. Sample set of CT images in DICOM format was generated using a commercially available 4D-XCAT digital phantom. Spherical tumors with diameters of 3 cm and 4 cm were generated in the CT images. These tumors were located in the upper and lower lobes of both lungs, which were then considered as the clinical target volume (CTV). The planning target volume (PTV) was then defined by adding an appropriate margin to the CTV based on the RT techniques (MR-linac or conventional).

These phantom and tumor data files were converted to the Geant4 geometry format. MC-based engine was used as the platform of treatment planning to calculate the dose distributions in the tumors and surrounding lung tissue for both MR-linac and conventional RT techniques. For all treatment plans, the prescribed doses were assumed to be 60 Gy. Analysis of the normal lung tissue complications for each RT technique was assessed according to the mean lung dose (MLD), percentage of the lung volume receiving doses of > 20 Gy (V_{20}), and the normal tissue complication probability (NTCP) of the lung.

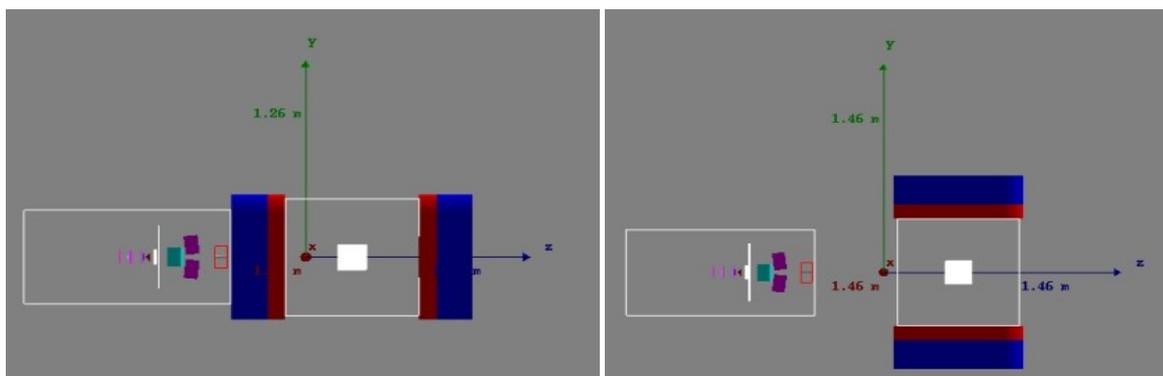
Results

The results show that the MLD, V_{20} and EUD were significantly lower for MR-linac RT especially for the parallel configuration. The largest reduction of MLD, V_{20} and EUD for MR-linac RT configurations were 5 Gy, 29.3% and 4.1 Gy, respectively. In addition, the present study suggests

that the MR-linac technique improved the NTCP value up to 15% and 7.5% for right and left lung, respectively.

Conclusions

To conclude, considering a smaller CTV-to-PTV margin in MR-Linac technique can compensate perturbations on the dose distributions in the presence of a magnetic field and will lead to lower complications in normal lung tissue compared to the conventional RT.



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Evaluation of a radiotherapy-dedicated Monte Carlo environment (PRIMO) for verification of clinical SBRT-VMAT plans for brain and lung metastases.

L. Paganini¹, G. Reggiori¹, A. Stravato¹, A. Fogliata¹, V. Palumbo¹, P. Mancosu¹, S. Tomatis¹

¹ *Humanitas Research Hospital, Rozzano, Italy*

Introduction and Aim

Since 2014 our institute is involved in PRIMO's beta-testing for its application in radiotherapy. PRIMO [1] is a graphical environment for MonteCarlo (MC) simulations based on the Dose Planning Method (DPM), a fast MC algorithm specifically built for the simulation of the deposited dose in radiotherapy. The objective of this work was to validate the beams calculated by DPM against the ones from our Linac EDGE (Varian) and to compare PRIMO with the clinical algorithm Acuros (Varian) and film measurements.

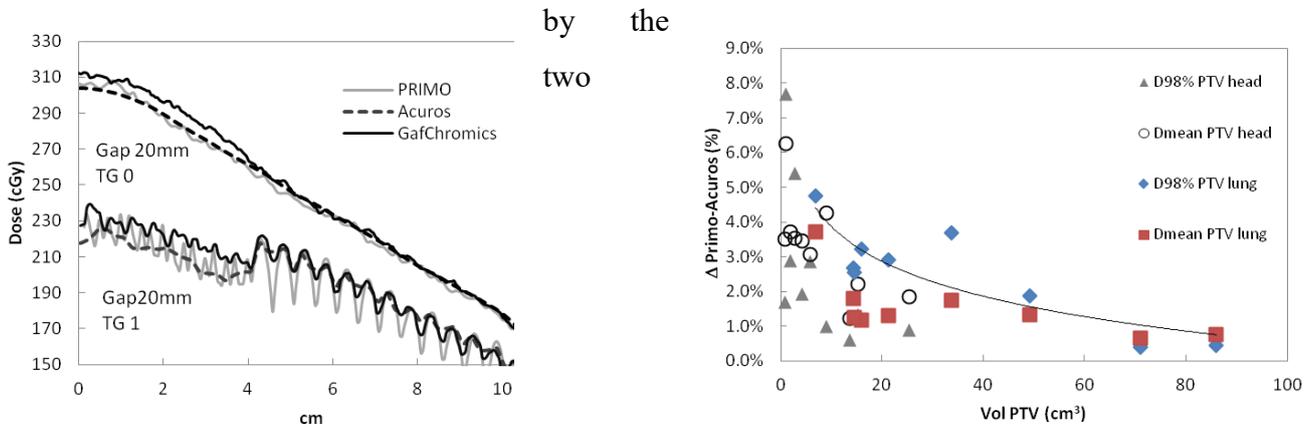
Materials and Methods

In a first phase a full characterization of the Millennium MLC beams was performed. Then the MLC modeling, particularly the Tongue and Groove effect, was investigated with two types of tests: static MLC fields in different settings and MLC plans configured in 'dynamic fence patterns'[2]. These dynamic tests were planned with increasing leaf ends gap size and degree of TG effect. The dose distributions were measured using the IBA MultiCube water-equivalent slab phantom with GafChromic films positioned horizontally at 10 cm depth. Finally a set of 20 SBRT metastatic patients was selected from our database (10 brain and 10 lung). For all patients VMAT plans were optimized with 10 MV FFF beam in Eclipse and calculated with Acuros. The DICOM files (plan, structures and images) were imported in PRIMO. DPM was used to calculate dose distribution in the patients. The dose distributions were compared in terms of gamma analysis within the BODY structure (3%, 2mm) and specific PTV dosimetric parameters (i.e. D98%, D95%, D2%, D5% and Dmean).

Results

Concerning the MLC modelling, static fields showed a good agreement between Acuros and PRIMO, with slight differences in TG, leaf-end transmission and transmitted dose. The comparison between dose profiles for the dynamic fields (Fig1) highlighted differences between measurements and calculations up to 8% for Acuros and 4% for PRIMO, in modelling the MLC central region where leaves are thinner and thus TG effect more consistent. Differences in the external part of the MLC are below 3% for both algorithms. The Gamma Agreement Index (GAI) between PRIMO and Acuros was calculated for the dose distributions for all the clinical plans obtaining values of 98.85%±0.5 for the brain and 97.51%±1.5 for the lung SBRT plans. The GAI increases with

increasing PTV volume (i.e. field size) (Fig2) for all the dosimetric parameters in the PTV. For field sizes $>2.5\text{cm}^2$ differences are $<3\%$ while differences are higher for the small targets. This is due to the sum of two effects: the critical TG modeling for the thinner leaves and the small field handling



algorithms.

1. Profile for dynamic test Gap 20mm and TG fractions 0 and 1.
2. Differences between PRIMO and Acuros for dosimetric parameters for clinical plans fitted with a logarithmic curve.

Conclusions

This preliminary study showed differences between PRIMO and Acuros in the MLC modeling, in particular regarding the TG effect for the smaller leaves, nevertheless PRIMO profiles are in good agreement with film measurements. The clinical plans show also an acceptable agreement in both anatomical regions. Possible material-related issues in the lung patients should be further investigated with PRIMO developers. PRIMO can be an interesting and simple tool to help the fine tuning of the TPS parameters in conditions where experimental measurements have high uncertainties and could benefit from simulations.

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Rotational radiotherapy of breast cancer with kilovoltage microbeam

V. Pirozzi Palmese^{1,2}

¹*Universita' di Napoli Federico II, Dipartimento di Fisica "Ettore Pancini", Napoli, I-80126, Italia.*

²*INFN Sezione di Napoli, I-80126, Italia*

Introduction and Aim

Microbeam RadioTherapy (MRT)^[1] is an innovative experimental technique that uses the dose-volume effect: normal tissue shows a high tolerance at the dose of several hundred Gy, delivered in a very small volume. For the first time, we investigated MRT as a new technique for breast radiotherapy with kilovoltage radiation in a rotational scan, by analysing simulated 3D dose distribution in a cylindrical PMMA phantom.

Materials and Methods

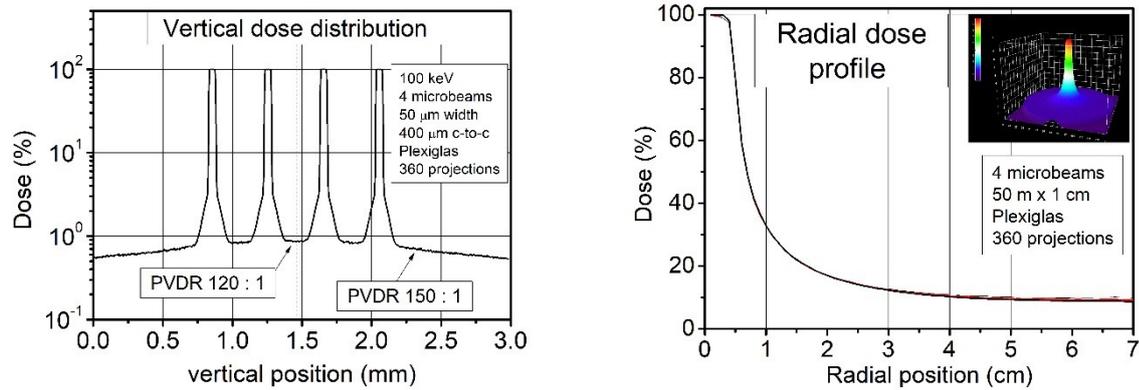
We developed a Monte Carlo (MC) code based on Geant4 toolkit, in order to evaluate the planar and vertical dose profile, and the Peak to Valley Dose Ratio (PVDR) in a projection irradiation, as well as the 3D dose distribution in a partial or fully tomographic irradiation. The PMMA cylindrical phantom of 14 cm diameter simulated the pendant breast of the patient in prone position. The source was a rectangular parallel monochromatic beam in the energy range from 80 to 120 keV, passing through a tungsten comb collimator (4 mm thick) with slit width 50 μm and slits separation of 400 μm centre-to-centre. A physical collimator is under realization via electro-discharge manufacturing.

Results

We calculated the dose deposition at 80, 100 and 120 keV for planar and rotational geometry. The primary source is modelled in four beamlets, each one of 1cm x 50 μm . The PVDR is estimated from the vertical dose profile calculated in central ROI (region of interest). At the beam centre the PVDR is about 120 : 1 and 150 : 1 in the periphery region. The radial dose profile (in an axial view) shows a rapid decrease: 17 % at 2 cm from the central target, as seen in the figure below.

Conclusions

We made a preliminary step towards the implementation of MRT technique with circular or spiral orbit in a partial or fully tomographic irradiation, for breast cancer radiotherapy. The simulations indicated an acceptable skin sparing effect. Indeed, in rotation irradiation mode tumour-to-skin dose ratio is about 9% for a central-mass at 80, 100 and 120 keV. The PVDR decreases from the beam centre to the periphery. In the future we will investigate the microbeam with LINAC generated the broad beam.



a)

b)

Figure: Dose profile obtained simulating a microbeam with four beamlets: a) vertical dose at 100 keV; b) radial dose profile for the three energies (80, 100 and 120 keV), they are perfectly overlapping.

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Respiratory-induced tumor motion evaluation with 4D-CBCT: are PTV margin related to tumor position necessary in a lung SBRT setting?

G. Della Gala^{1,2}, S. Pini², S. Russo², M. Esposito², L. Paoletti², P. Alpi², R. Barca², M. Coppola², S. Fondelli², F. Rossi², P. Bastiani²

(1) Scuola di Specializzazione in Fisica Medica, Università degli Studi di Firenze, Firenze

(2) USL Toscana Centro, Firenze

Introduction and Aim

4D-CBCT has been increasingly used to evaluate lung tumor position and to validate the PTV margins during the course of the treatment. This is particularly important in SBRT where high doses are delivered to small targets[1].

Materials and methods

This study is a retrospective analysis on patients treated with lung SBRT. 4D-CT scans for planning were obtained on a GE Bright-Speed 4D-CT scanner. For breath control a compression abdominal belt was used. GTV was contoured on each of the multi-phases reconstructed images to generate ITV and PTV (ITV plus 5mm). Prior to each fraction, in-room 4D-CBCT image scan was acquired and registered to the planning CT by the Symmetry XVI Elekta system using an automatic two steps image registration (dual registration): first an anatomical landmarks-based clipbox was defined for setup correction and then a mask of 5mm around PTV was created for the soft tissue registration[2,3]. Matching results were used to shift the table along the x-y-z directions (that is respectively left-right, superior-inferior, and anterior-posterior) to correct daily patient setup and tumor baseline shifts. The dual registration results were always reviewed by the physician and manually adjusted if not correct. The baseline shifts were measured by subtracting the clipbox suggested correction from the applied table shift. Tumour motion was quantified for each fraction as the absolute range of the respiratory cycle; the inter-fraction variability of the target motion was therefore assessed for each patient as the difference between the max and min intra-fraction ranges. All the previously mentioned parameters were considered both globally and dividing the patients based on the position of the tumor in the lung (upper/middle/lower lobes). To evaluate the performance of the XVI System, applied table shifts that differed from the dual registration were recorded.

Results

59 patients receiving lung SBRT (276 fractions in total) between January 2016 and June 2018 were included. A large inter-fraction baseline shifts of lung tumours was observed. 11/59 patients showed a baseline shift higher than 5 mm in at least one fraction of the treatment course, mainly along y and z. The inter-fraction variability of respiratory-induced tumor motion was higher than 5 mm in at least one direction for 10/59 patients (max: 20 mm along the y direction) and, with one exception, always along y and z. As expected, the variability was particularly significant for patients with a lesion in the lower lobe. The applied shift differed from the automatic soft-tissue registration in 8% of the fractions (1% higher than 5 mm). All the differences were scored for patient with target in the lower or middle lobe.

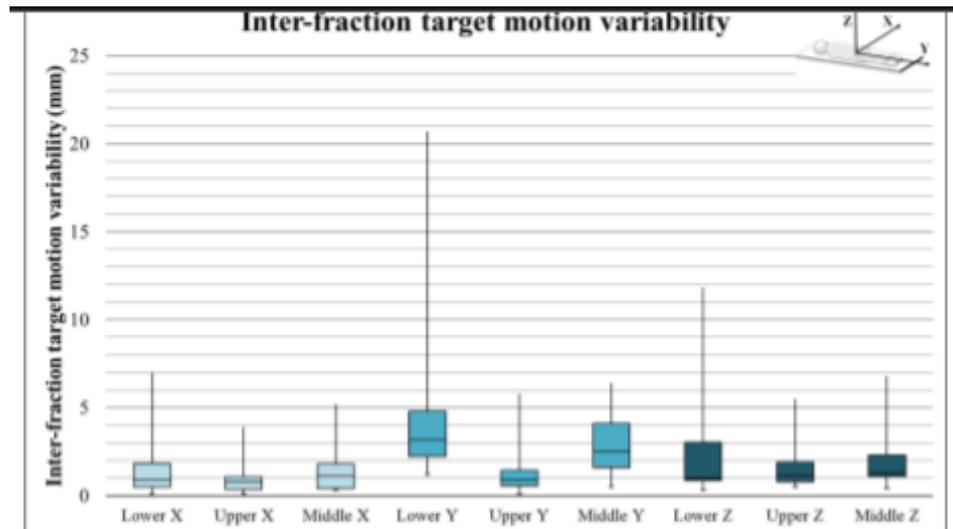


Fig. 1: Box plot of the absolute inter-fraction target motion of the tumor along the three directions based on the position of the tumor in the lung. Higher ranges are visible for tumors positioned in the lower lobe of the lung.

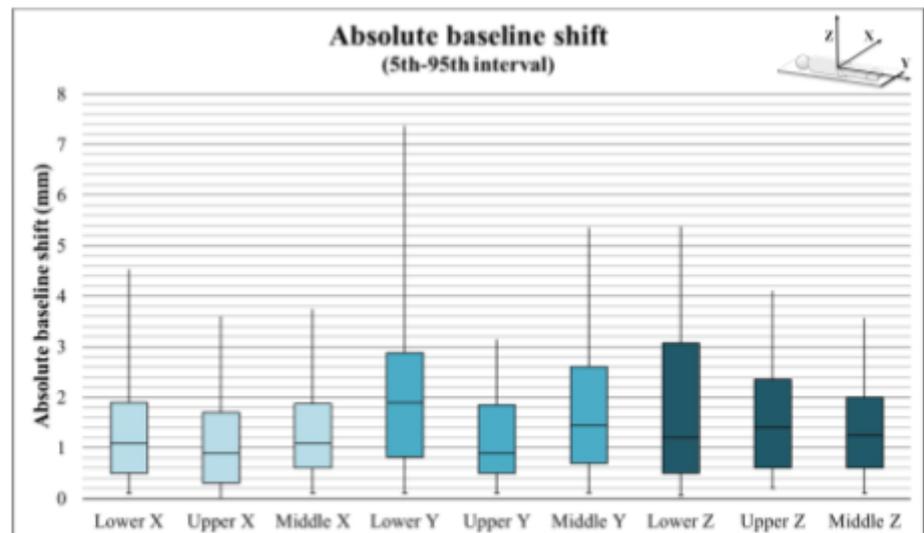


Fig. 2: Box plot of the absolute baseline shift of the tumor along the three directions based on the position of the tumor in the lung. The shift is more pronounced for tumor positioned in the lower lobe of the lung for all the directions.

Conclusions

4D-CBCT allows an accurate target localization that is necessary to correct the patient positioning based on the daily not negligible baseline shift of the tumor. This preliminary analysis suggests the need for the definition of PTV margins according to the position of the tumor inside the lung due to

the different respiratory-induced motion. Review of 4D-CBCT automatic registrations by a physician is recommended.

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Study to evaluate the impact of calculation grid resolution and CT slice thickness on TPS calculated small fields OF

M.D.Falco¹, S.Clemente¹, C. Fiandra¹, R.Consorti¹, G. Benecchi¹, C. Carbonini¹, M. Casale¹, F.R. Giglioli¹, E. Gallio¹, M. Casati¹, A. Delana¹, M. Fusella¹, S. Linsalata¹, T. Malatesta¹, G. Reggiori¹, E. Villaggi¹, S. Russo¹, P. Mancosu¹

¹SBRT Working Group, AIFM - Italian Association of Medical Physics, Italy

Introduction and Aim

Stereotactic Body Radiation Therapy (SBRT) for patients with early stage solid tumor is increasing. We present results of a national study to evaluate the influence of calculation grid resolution and CT slice thickness on TPS calculated small fields output factors (OFs) using a homogeneous phantom.

Materials and Methods

Twenty-eight centres of the Italian Association of Medical Physics (AIFM) SBRT working group, with different LINAC/TPS combinations, were enrolled in the study. A preliminary dataset based on thirteen centres were analysed. Each center received 3 CT scans of different slice thickness, i.e. 1,2 and 3 millimetres. OFs calculated using the TPS commissioning setup 1x1 cm², 2x2 cm² and 3x3 cm² field sizes normalized to 10x10 cm² field, in the following combination: 1 mm grid resolution and 1 mm slice thickness (G1/S1), 1 and 2 mm grid resolution and 2 mm slice thickness (G1/S2 and G2/S2, respectively), 1,2 and 3 mm grid resolution and 3 mm slice thickness (G1/S3, G2/S3 and G3/S3, respectively) were collected. Data were compared to OF measured. The percentage differences between OFs measured and calculated by TPS, were analysed.

Results

Results showed on average, OFs calculated by TPSs larger than OFs commissioned. These deviations increased with decreasing of field size.

The largest discrepancies were observed using G3/S3 combination for 1x1 cm² field size and Varian/Eclipse

LINAC/TPS combination.

In particular, for this combination, we found

Field Size (cm ²)	LINAC/TPS combination	G/S combination	Max Percentage Discrepancy (%)
1x1	Varian/Eclipse	G3/S3	-11
1x1	Elekta/Monaco	G1/S2	-3.2
1x1	Elekta/Masterplan	All G/S combinations	-5
1x1	Varian/Pinnacle	G3/S3	-5.9
2x2	Varian/Eclipse	G3/S3	-3.5
2x2	Elekta/Monaco	G1/S3	-3.7
2x2	Elekta/Masterplan	All G/S combinations	-1.8
2x2	Varian/Pinnacle	G1/S1	0.0

Table 1: Maximum percentage discrepancies observed ((Measured Dose - Calculated by TPS Dose)/Measured Dose*100) as a function of field size, grid resolution/slice thickness combination (G/S) and LINAC/TPS combination, respectively.

that discrepancies were mainly dependent on grid resolution rather than slice thickness and increased with grid resolution. Similar results were found for Varian/Pinnacle combination, even if the max percentage discrepancy for 1x1 cm² field size was lower than Varian/Eclipse combination ($\Delta=-5.9\%$). As regards Elekta/Masterplan, we found a weak influence of slice thickness and grid resolution on OF calculation. On the other hand, Masterplan does not allow in TPS modeling measured OFs corresponding to fields lower than the 5x5 cm². Finally, as regards Elekta/Monaco, we obtained a large dispersion of the data provided by the users of the TPS Monaco, that can be partly attributed to non-homogeneous calculation methods (variance of the VMC algorithm) and how the calculated data are collected (radius of the dose point). A summary of these results is presented in Table 1.

Conclusions

We studied the influence of the dose calculation resolution and CT slice thickness on small OFs. Our results indicate that modern TPS beam models overestimate the OFs for small fields with greater differences with respect to measured OFs at greater slice thickness and grid resolution. These variations seem to be larger for Varian/Eclipse combination than Varian/Pinnacle or Elekta/Masterplan or Elekta/Monaco combinations, respectively. In particular, for Monaco, the effect of the variance of the VMC algorithm on OF calculated is under investigation.

Evaluation of Knowledge Based Planning applied to prostate SBRT

M. Fusella ¹, A. Scaggion ¹, M. Sepulcri ², E. Villaggi ³, M. Paiusco ¹

¹ *Department of Medical Physics, Veneto Institute of Oncology IOV – IRCCS, Padua, Italy*

² *Department of Radiation Oncology, Veneto Institute of Oncology IOV – IRCCS, Padua, Italy* ³
Medical Physics Unit, AUSL Piacenza, Italy

Introduction and Aim

Large variations of radiotherapy treatment quality have been observed between institutions or among planners and could be mainly attributed to the operator's experience. This has a great impact on hypofractionated treatments, where the planning experience was found to be correlated with disease outcome [1]. Knowledge Based Planning (KBP) has been suggested as a solution to reduce this variation in single and multi institution environment [2]. In this work a KBP model trained on standard fractionation prostate treatments has been applied to patient elected for SBRT schedule.

Materials and methods

A KBP model was trained on seventy patients treated for radical prostate cancer. [3] All the patients were treated with VMAT to deliver 78 Gy or 70 Gy to the PTV over 39 or 28 fractions. Five anonymized patients elected for SBRT treatment, taken from [4], were used as test sample for the prediction of the KBP model. A single optimization process without human intervention was performed to avoid any bias due to planner intervention, to deliver 35 Gy in five fractions. Dosimetric quality of plans were compared with the data published in [4]: Dmean, D98 and D2 for PTV, V32Gy, V28Gy and V18Gy, for rectum, and V30Gy and V18Gy, for bladder were considered. A t-test was performed comparing published results and data of the present study.

Results

Two out of five patients lied outside the domain of the KBP model so the predictions of their DVH might have been not correct. Nevertheless the plans showed a satisfying DVH for all the organs at risk of all the 5 patients. Comparing our results with data published in [4], only PTV's Dmean resulted statistically different, with 1% lower coverage for KBP plans ($p < 0.001$). All the other DVH points did not show any statistically significant difference.

Conclusions

We applied a KBP model trained with standard dose schedule (2 Gy/fx and 2.5 Gy/fx) to patients treated in SBRT regimen (7 Gy/fx) to obtain DVH predictions. Automatic optimization based on those predictions produced valuable plans which resulted comparable with previously published ones. Further refinement of the KBP model can be obtained using a crowd-knowledge approach in a multi-institutional study for the fine tuning of the optimization process (i.e. Dmean of the PTV).

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To evaluate effects of inaccurate small fields output factors measurements on stereotactic brain volumetric modulated arc therapy (VMAT) plans: first results

M. Boccia⁷, M.D. Falco¹, S. Clemente², C. Talamonti³, E. Cagni⁴, A. Alparone⁵, S. Russo⁶, F. Foppiano⁸, E. Gino⁹, F. Rosica¹⁰, M. Stasi⁹, C. Fiandra¹¹

¹	<i>Policlinico</i>	<i>SS.</i>	<i>Annunziata,</i>	<i>Chieti,</i>	<i>Italy</i>
²	<i>AOU</i>	<i>Federico</i>	<i>II,</i>	<i>Napoli,</i>	<i>Italy</i>
³	<i>AOU</i>	<i>Careggi,</i>	<i>Firenze,</i>	<i>Italy</i>	
⁴	<i>AUSL-IRCCS,</i>	<i>Reggio</i>	<i>Emilia,</i>	<i>Italy</i>	
⁵	<i>Tecnologie</i>	<i>Avanzate,</i>	<i>Torino,</i>	<i>Italy</i>	
⁶	<i>Azienda</i>	<i>USL</i>	<i>Toscana</i>	<i>Centro,</i>	<i>Firenze,</i>
⁷	<i>Centro</i>	<i>Polidiagnostico</i>	<i>Check-Up,</i>	<i>Salerno</i>	
⁸	<i>ASL n.5 "Spezzino", La Spezia</i>				⁹
<i>AO</i>	<i>Ordine</i>	<i>Mauriziano</i>	<i>Torino</i>		
¹⁰	<i>P.O.</i>	<i>Mazzini</i>	<i>ASL,</i>	<i>Teramo</i>	

¹¹ *Università di Torino, Italy.*

Introduction and Aim

To evaluate the effects on calculated doses if inaccurate small fields output factors (OFs) measurements were used in treatment planning dose calculation.

Materials and Methods

This multi-institutional study (eight centers with eight different LINAC-TPS combinations) was drawn on different phases. In the first, a baseline stereotactic brain plan for each center was acquired. For the purpose, CT data for a single brain metastasis was selected and shared among all centers. Planning rules, beams geometry and calculation grid (1mm) were the same for all centers. All DICOM RT plans, were analyzed into PlanIQ software (SUN NUCLEAR) and scored by means of a quantitative total scorecard based on clinical goals. Then, according to the equation by Sauer and Wilbert [1], OFs for field sizes ranging from 1x1 to 3x3 cm² were gradually changed from $\pm 3\%$ to $\pm 1\%$ increments compared to the commissioned OFs. For each center, two new machines models called OFup and OFdown (for positive and negative increment respectively) were generated. Then each plan was recalculated using the "incorrect" OFs and compared to the baseline plan. The same study on multiple lesions is underway.

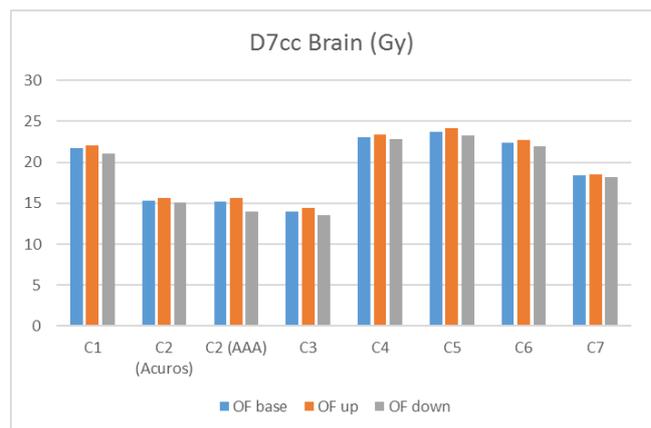
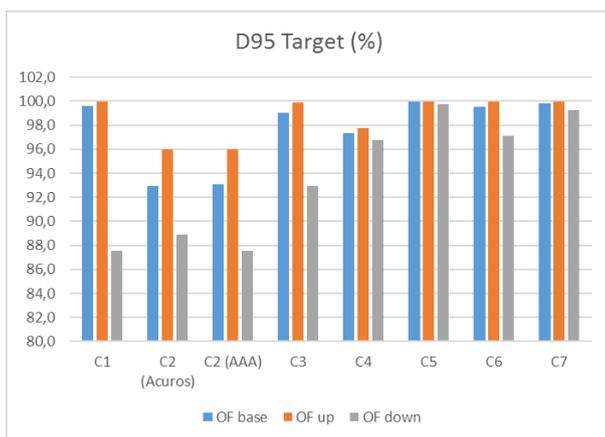
Results

PlanIQ analysis was performed identifying plan quality metric components and goals as for target well as for OARs. All baseline plans reached the prefixed cumulative percentage performance

quality metric (PMQ) fixed to 80%. The same trend in target coverage (D95) was observed between centers (Figure 1) using OFup and OFdown with a slight discrepancy in D95 using the OFdown. No significant difference was found with regard to OARs sparing (Figure 2). Preliminary data on multiple lesions showed a larger difference in D95 using OFup and OFdown compared to baseline data depending on targets diameter. No significant difference was found with regard to OARs sparing too.

Conclusions

This is among the few studies in literature that investigate the impact of small field OF inaccuracies on clinical plans. Our preliminary results will be connected to the different TPS, linacs, MLCs and targets used. At moment, the bigger impact on using incorrect OFs seems related to the target coverage and less to OARs sparing.



References:

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Performances evaluation of a tumor motion management system with ADAM, a breathing anthropomorphic phantom

S. Calusi^{1,2}, R. Lisci³, L.Masi², C. Talamonti^{1,4}, L. Marrazzo⁴, L.Foggi¹, L.Livi^{1,5}, G.Simontacchi⁵, S. Pallotta^{1,4}

¹ *University of Florence, Department of Biomedical, Experimental and Clinical Sciences “Mario Serio”, Florence, Italy*

² *Department of Medical Physics and Radiation Oncology, IFCA, Florence, Italy*

³ *University of Florence, Department of Agricultural, Food and Forestry System, Florence, Italy*

⁴ *Medical Physics Unit AOU Careggi, Florence, Italy*

⁵ *Radiotherapy Unit AOU Careggi, Florence, Italy*

Introduction and Aim

In this work we present end-to-end (E2E) tests results of the tumor motion management arrangement of a robotic radiosurgery system using different respiratory signals produced by ADAM, an home-made breathing anthropomorphic phantom.

Materials and Methods

The tested system uses a model that correlates the external respiratory signal, coming from three light-emitting diodes fixed on the thorax, and the internal tumor position derived from two orthogonal images acquired using two in-room X-ray tubes and detectors. The correlation model and a prediction algorithm are employed to define the position of the tumor during treatment. ADAM is an anthropomorphic phantom containing realistic anatomical structures and capable of different breathing patterns and respiratory signals. E2E tests were performed using a 3D printed openable cube containing a sphere, included in a solid foam block simulating lung, as a tumor-like structure. Two orthogonal EBT3 films where inserted in the sphere and a treatment plan conformed to the sphere was delivered using the tumor motion management system while moving the sphere and the thorax of ADAM according to four different respiratory traces: a) linear and b) elliptical paths with a shorter inhale than exhale with the thorax moved in sync; c) linear path dephasing thorax motion and d) linear path based on a real patient breathing signal with the thorax moved in sync. The plan was also delivered in static condition to be used as a reference and, as a last test, it was delivered using the patient trace d), but the tracking was deactivated. For all tests the uncertainty in the detection of the sphere, provided by the tracking algorithm, was observed and compared with that one obtained in real patient cases. Films were analyzed and the global tracking error, expressed by the distance between the centroid of planned and delivered dose distributions,

was measured. Moreover, a film dosimetry analysis that compares films irradiated in static and moving conditions was performed.

Results

The 3D printed sphere was detected by the tumor tracking algorithm with a detection uncertainty in the range 10%-20% for both orthogonal images, similar to that observed in real patient treatments (15.5% average). Tracking errors derived for the four tested respiratory traces and the static condition were all below 0.95 mm (range 0.6-0.9 mm). The maximum difference in tracking error between two repeated tests using the same delivery conditions was 0.4 mm. Gamma passing rates resulted above 90%, considering 3%/1 mm local criteria for all respiratory traces using tracking while it dropped below 50% when the tracking system was deactivated.

Conclusions

The phantom complexity enables to test the robotic system capability in detecting tumor in a scenario similar to that met in real patient cases. The performances of the tracking system resulted within the tolerance levels also using an anthropomorphic capable of complex respiratory patterns.

Helical Tomography radiation therapy of multiple brain lesions: in-phantom accuracy assessment

M.Zani¹, L. Marrazzo², S.Calusi¹, C.Talamonti^{1,2}, S.Scoccianti³, D.Greto³, I.Desideri³, F.Fusi¹, S.Pallotta^{1,2}

¹ *University of Florence, Department of Biomedical, Experimental and Clinical Sciences “Mario Serio”, Florence, Italy*

² *Medical Physics Unit AOU Careggi, Florence, Italy*

³ *Radiotherapy Unit AOU Careggi, Florence, Italy*

Introduction and Aim

Aim of the present study was to evaluate the accuracy which can be obtained with helical tomography radiation therapy (HT) systems in the case of multiple intracranial targets treatments.

Materials and Methods

In HT systems target localization is provided by registering MegaVoltage CT (MVCT) and CT images. The registration can be performed manually and by means of an automatic registration software which employs a modified version of the mutual information algorithm on the entire image. Moreover two options, where the registration algorithm uses only voxels with a density $> 1.1 \text{ g/cm}^3$ and between 0.3 and 1.1 g/cm^3 to focus on bone and bone and soft tissues respectively, are available. Its accuracy depends on MVCT acquisition protocols and on image registration algorithms. Set-up accuracy was measured, for different registration options and MegaVoltage CT (MVCT) slice thickness, by applying known misalignments to an ad-hoc developed phantom. End-to-End (E2E) tests were performed to assess the delivery accuracy in phantoms containing multiple targets by using radiochromic films: measured dose distribution centroids were compared with physical and calculated target positions on axial and coronal planes. A Gamma index analysis was carried out on planned and measured planar dose maps.

Results

The algorithm focusing on bone and tissues with the fine MVCT reconstruction grid gave the best results among the automatic options. The most accurate registration modality resulted to be the manual one with a sub-voxel accuracy shifts and a capability in the detection of rotations within 0.3° . For the E2E along the coronal plane (6 targets), a mean deviation between measured dose distribution centroids and physical barycenters of 0.6 mm (range 0.1 mm-1.3 mm) was observed. Along the axial plane (5 targets), a mean deviation of 1.2 mm (range 0.7 mm-2.1 mm) was found for the centroids shifts. Gamma index (3%/2 mm, local) passing rates higher than 97% between planned and delivered dose distributions were measured.

Conclusions

These results demonstrate that multiple brain lesion HT treatments are feasible with an accuracy at least comparable to frameless linac-based irradiation, when a set-up capable to assure angular corrections and a reliable patient immobilization are employed.



