Table 11 Annual number of new cancer patients by disease site※7

原発巣	新患者数	(%)
脳・脊髄腫瘍	9,061	(5.3)
頭頸部腫瘍（甲状腺腫瘍を含む）	18,105	(10.6)
食道癌	9,594	(5.6)
肺癌、気管・縦隔腫瘍	32,307	(18.9)
うち肺癌	29,191	(17.0)
乳癌	39,834	(23.3)
肝・胆・膵癌	6,641	(3.9)
胃・小腸・結腸・直腸癌	8,279	(4.8)
婦人科腫瘍	8,216	(4.8)
泌尿器系腫瘍	23,050	(13.5)
うち前立腺癌	17,919	(10.5)
造血器リンパ系腫瘍	7,949	(4.6)
皮膚・骨・軟部腫瘍	4,093	(2.4)
その他（悪性腫瘍）	1,941	(1.1)
良性腫瘍	2,220	(1.3)
15歳以下の小児例（上記と重複）	1,092	(0.6)
合計	171,290	(100)

※7 原発巣別新患者数が未記入の施設があったため，合計がTable 4-1の新患者数の合計と異なっている。

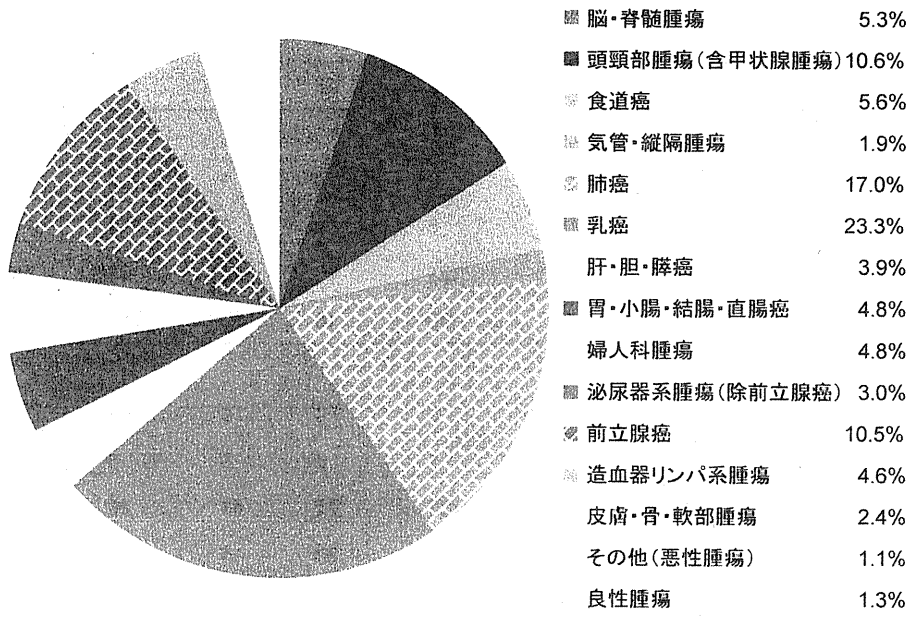

Figure 3. Annual number of new cancer patients by disease site※7

※7 原発巣別新患者数が未記入の施設があったため，合計がTable 4-1の新患者数の合計と異なっている。

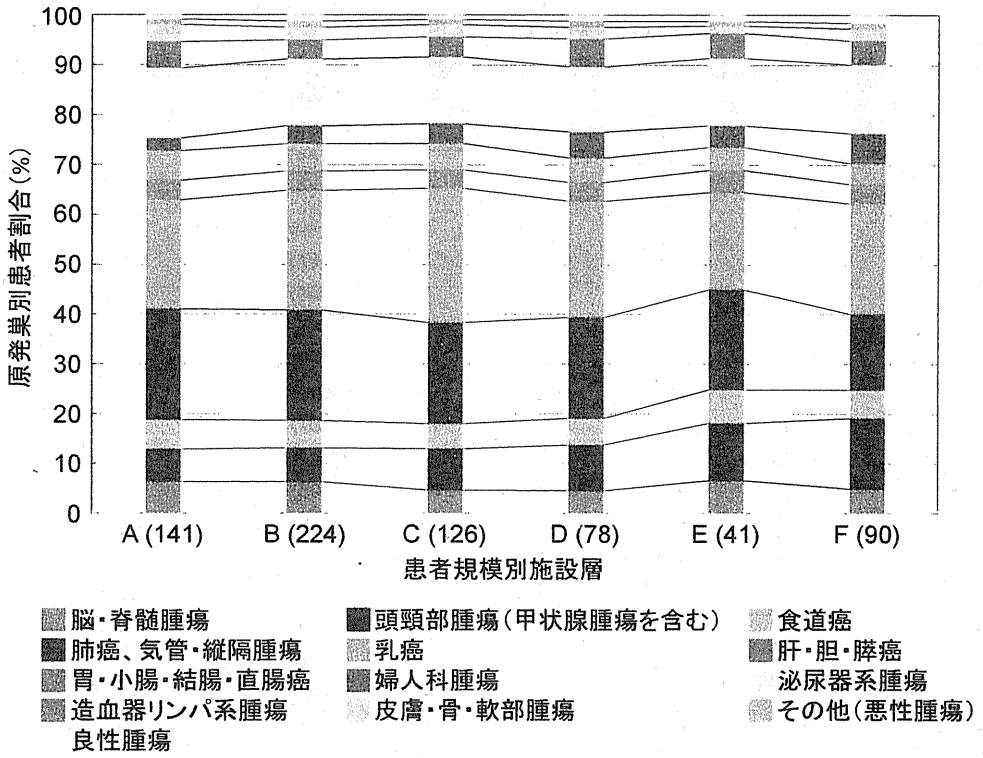

Figure 4. Distribution of annual number of new cancer patients by disease site by patient load of radiation oncology facilities.

Table 12 Annual number of total cancer patients (new + repeat) treated for any of brain metastasis and bone metastasis by patient load of radiation oncology facilities

転移	実患者数 (放射線治療実患者総数に対する割合 [%])						
	A (141)	B (224)	C (126)	D (78)	E (41)	F (90)	Total (700)
脳転移	869	4,206	3,203	3,664	2,574	5,818	20,334
	(8.7)	(11.2)	(8.5)	(11.5)	(11.7)	(7.4)	(9.3)
骨転移	1,416	5,593	5,278	4,397	2,078	8,144	26,906
	(14.2)	(14.9)	(14.1)	(13.8)	(9.4)	(10.3)	(12.4)

Table 13 Number of patients, facilities, and certified personnel according to prefecture

都道府県名	人口[13)] 単位: 千人	放射線治療新患数 (人口千人当新患数)		治療施設数 (1施設当人口: 千人)		施設当たりの 放射線治療新患数	JASTRO 認定医数
北海道	5,507	9,235	(1.7)	30	(184)	307.8	27
青森県	1,379	1,880	(1.4)	10	(153)	188.0	7
岩手県	1,340	1,514	(1.1)	9	(168)	168.2	5
宮城県	2,336	3,916	(1.7)	13	(212)	301.2	11
秋田県	1,096	1,680	(1.5)	11	(110)	152.7	1
山形県	1,179	1,332	(1.1)	7	(197)	190.3	5
福島県	2,040	2,832	(1.4)	9	(204)	314.7	5
茨城県	2,960	3,520	(1.2)	16	(197)	220.0	8
栃木県	2,006	2,510	(1.3)	10	(251)	251.0	7
群馬県	2,007	3,318	(1.7)	14	(154)	237.0	19
埼玉県	7,130	6,659	(0.9)	19	(357)	350.5	17
千葉県	6,139	7,022	(1.1)	24	(267)	292.6	30
東京都	12,868	24,182	(1.9)	73	(195)	331.3	69
神奈川県	8,943	11,742	(1.3)	38	(248)	309.0	31
新潟県	2,378	3,576	(1.5)	13	(170)	275.1	5
富山県	1,095	1,500	(1.4)	8	(137)	187.5	5
石川県	1,165	1,838	(1.6)	8	(166)	229.8	4
福井県	808	1,144	(1.4)	6	(135)	190.7	4
山梨県	867	1,036	(1.2)	4	(217)	259.0	5
長野県	2,159	3,055	(1.4)	15	(144)	203.7	6
岐阜県	2,092	2,858	(1.4)	10	(174)	285.8	5
静岡県	3,792	5,586	(1.5)	27	(165)	206.9	17
愛知県	7,418	10,043	(1.4)	37	(195)	271.4	20
三重県	1,870	1,827	(1.0)	13	(156)	140.5	4
滋賀県	1,405	1,724	(1.2)	11	(141)	156.7	4
京都府	2,622	3,789	(1.4)	14	(202)	270.6	15
大阪府	8,801	13,201	(1.5)	51	(176)	258.8	45
兵庫県	5,583	7,738	(1.4)	35	(174)	221.1	26
奈良県	1,399	1,937	(1.4)	7	(175)	276.7	8
和歌山県	1,004	1,509	(1.5)	9	(100)	167.7	4
鳥取県	591	1,049	(1.8)	6	(84)	174.8	2
島根県	718	936	(1.3)	5	(144)	187.2	6
岡山県	1,942	2,803	(1.4)	11	(177)	254.8	8
広島県	2,863	4,731	(1.7)	18	(159)	262.8	20
山口県	1,455	2,002	(1.4)	14	(104)	143.0	4
徳島県	789	1,353	(1.7)	3	(158)	451.0	3
香川県	999	1,090	(1.1)	6	(143)	181.7	4
愛媛県	1,436	2,189	(1.5)	12	(131)	182.4	8
高知県	766	1,226	(1.6)	6	(128)	204.3	3
福岡県	5,053	8,198	(1.6)	27	(194)	303.6	23
佐賀県	852	800	(0.9)	4	(213)	200.0	3
長崎県	1,430	2,157	(1.5)	8	(179)	269.6	4
熊本県	1,814	3,240	(1.8)	14	(130)	231.4	6
大分県	1,195	1,538	(1.3)	13	(109)	118.3	4
宮崎県	1,132	1,410	(1.2)	5	(162)	282.0	2
鹿児島県	1,708	2,289	(1.3)	12	(142)	190.8	5
沖縄県	1,382	1,676	(1.2)	6	(197)	279.3	5
合計	127,513	182,390	(1.3)	721	(182)	236.1	529

Table 14 Number of radiation oncology facilities, treatment devices, patient load and personnel: trend 1990-2009

	1990[1)]	1993[2)]	1995[3)]	1997[4)]	1999[5)]	2001[6)]	2003[7)8)]	2005[9)10)]	2007[11)12)]	2009
施設数	378	629	504	568	636	603	726	712	721	700
(回収率 [%])	(48.5)	(88.3)	(73.9)	(78.6)	(86.3)	(85.3)	(100)	(96.9)	(94.2)	(90.9)
新患者数	62,829	—	71,696	84,379	107,150	118,016	149,793	156,318	170,229	182,390
実患者数	—	—	—	—	—	—	—	191,173	205,087	217,829
施設平均新患者数	166	—	142	149	168	196	206	220	236	261
治療装置台数(稼働中)										
リニアック	311	508	407	475	626	626	744	765	807	816
テレコバルト	170	213	127	98	83	45	42	11	15	9
Ir-192 RALS	—	—	29	50	73	93	117	119	110	130
常勤放射線治療医数	547	748	821	889	925	878	921	1,003	1,007	1,085
FTE 放射線治療医数	—	—	—	—	—	—	—	774	826	939
常勤 JASTRO 認定医数	—	—	—	—	—	308	369	426	477	529
放射線治療担当技師数	592	877	665	733	771	918	1,555	1,635	1,634	1,836
周辺装置台数										
X 線シミュレータ	295	430	394	452	512	464	532	502	445	361
CT シミュレータ	30	75	55	96	164	247	329	407	497	575
治療計画コンピュータ	238	468	374	453	682	680	874	940	1,070	1,271

推定新患者数 2005: 約 16 万 2 千人(735 施設換算), 2007: 約 18 万 1 千人(765 施設), 2009: 約 20 万 1 千人(770 施設)
推定実患者数 2005: 約 19 万 8 千人(735 施設換算), 2007: 約 21 万 8 千人(765 施設), 2009: 約 24 万人(770 施設)

A4-2

Improvements in fabrication process of the patient bolus for prostate cancer used at particle therapy

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Keywords: Particle Therapy, Bolus, Treatment Planning

Purpose

We considered the redesign of the bolus fabrication processes to gain the prostate cancer patient throughput.

Method

The bolus resinous material was chemical wood both in the previous and present method. Same IGES outputs from TPS was used both in the present and previous methods. The difference in both methods is the choice of endmills and cut methods in machining centers. One endmill was adopted in the present one through the whole process, while several endmills were used in the previous one. Also cut speed were differed between two methods according to the different choice of endmills. The fabrication time and proton dose distribution were compared.

Result and Discussion

It took only one tenth in time in present method, while it took two and half hours in the previous one. No significant difference could be seen at the proton dose distributions.

This result suggests that the choice of endmills is not a matter of the precision in bolus fabrication. One can expect the time reduction in bolus fabrication without any quality losses.

Conclusions

The bolus fabrication process has been shown to reduce the bolus process time without significant dose distribution change.

◆Summary
Proton therapy and its profitability at the public hospital - the present status at six months after the opening of proton cancer therapy center
Proton therapy center in Fukui prefectural hospital opened on March 7th, 2011. Total 80 patients were treated by the end of October. It is estimated that 400 patients per year are needed to take profit. We have to make more efforts to increase the number of patients.

臨床・経営面での変化から見た機器稼働

公立病院での陽子線治療と採算性
陽子線がん治療センターオープン半年強を踏まえて

山本和高 ◈ 福井県立病院 陽子線がん治療センター

要旨：福井県立病院陽子線がん治療センターは2011年3月7日より診療を開始し、10月末までに80名の患者の陽子線治療を行った。採算のためには1年間に400名が必要と試算されており、患者数を増やす努力が不可欠である。

福井県立病院陽子線がん治療センターは、日本国内では7番目、日本海側では最初の陽子線がん治療施設として、3月7日より診療を開始した。

福井県には原子力発電所13基と高速増殖炉「もんじゅ」および「ふげん（廃炉）」があり、全国最多の原発立地県である。敦賀市にある若狭湾エネルギー研究センターでは福井県受託事業として陽子線がん治療高度化研究を実施し、2003年7月より陽子線がん治療臨床研究を行ってきた。福井県立病院陽子線がん治療センターは、その成果を引き継いで、主に、国からの電源立地地域対策交付金を利用して設置された。

陽子線がん治療センターの概要

福井県立病院は、JR福井駅から車で5分程度の福井市内の便利な場所にある診療科目19科、一般病床668床の総合病院で、がん診療連携拠点病院に指定されている。09年2月には、がん専門外来やがん専門病棟を有するがん医療センターが開設された。外来化学療法、内視鏡手術なども積極的に行っており、陽子線治療も含めて総合的かつ高度ながん治療を担っている。

陽子線がん治療センター（図1）は地上3階（一部4階）地下1階、延床面積5900㎡、病院本棟の北側に位置し、本棟とは地下廊下でもつながっている。図2は、陽子線がん治療センター1階の見取り図で、玄関を入ると受付があり、中央の待合ラウンジは吹き抜けになっていて、右側に診察室、左側に治療室がある。治療装置は三菱電機製で、入射器は直線加速器（RFQ+DTL）で7MeVまで加速し、主加速器のシンクロトロンは周長約20m、陽子を235MeVまで加速し、最大平均ビーム電流は10nA、最大線量率は5Gy/minである。治療室は、水平固定照射室が1室、回転ガントリーを備えた治療室が2室の合計3室である。

開設当初は回転ガントリーのある治療室2のみの稼働（図3）であったが、7月より水平固定照射の治療室1が稼働開始となり、それ以降は、前立腺がん症例は原則として治療室1で陽子線照射を行っている。治療室3には、CT自動位置決めシステムと積層原体照射システムという新しい機能が付加されており、薬事法の認可を申請するための基礎データの取得を進めている。2階には、CT、MRI、PET／CTの画像検査室と治療計画作成室が設置されている。固定具の作成はCT室で行っている。

治療計画ソフトはXio-N（三菱電機製）を使用。治療計画については、呼吸性移動がある部位は呼吸同期4D-CTを撮像。照射部位に応じて4D-PET／CT画像やMRI

画像を撮像し、治療計画作成の参考としている。地下に、患者ボーラスやコリメータを作成するためのＮＣマシーンやワイヤ・カッターを備えた工作室がある。

現在、放射線治療医４名、診療放射線技師７名、医学物理職３名、看護師２名、受付等の事務職員３名で陽子線治療センターの業務を行っており、加速器の運転やメインテナンス等は三菱電機に委託している。ＮＣマシーンやワイヤ・カッターの操作も外部委託している。

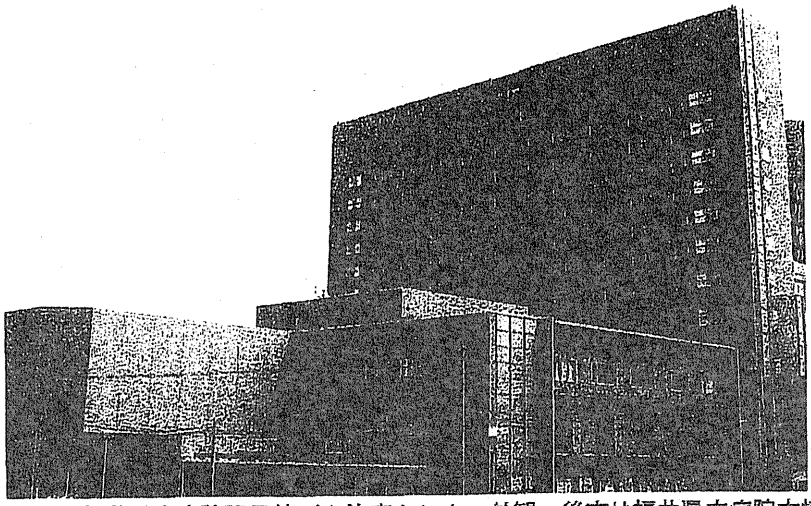

図１　福井県立病院陽子線がん治療センター外観　後方は福井県立病院本棟

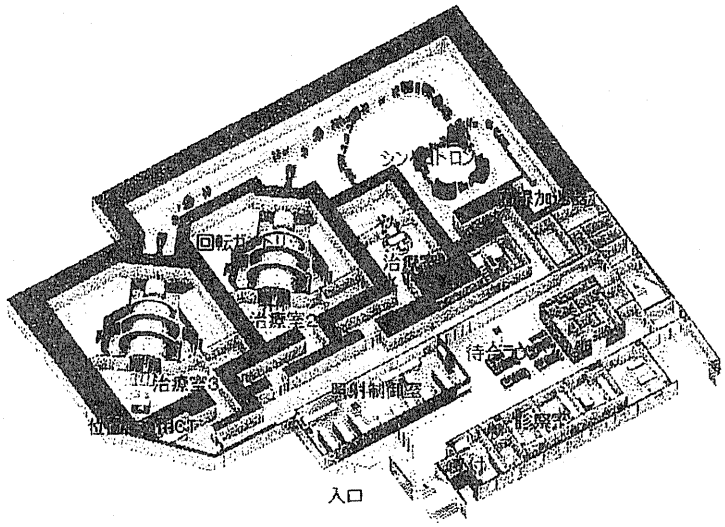

図２　福井県立病院陽子線がん治療センター　１階見取り図

図３　治療室２　陽子線照射準備中

陽子線がん治療の状況
―対象疾患・治療費・患者数について

陽子線がん治療の対象疾患としては、頭頸部腫瘍、非小細胞肺がん、肝臓がん、前立腺がん、転移性腫瘍に対し治療基準を作成し、ホームページ等で公表している。陽子線治療を希望する患者がこの基準を満たしている場合は、十分に陽子線治療について説明し、同意を得た後に陽子線治療の準備を始めている。治療基準を満たしていない場合でも、陽子線治療の適応があると考えられる症例については、病院内のキャンサー・ボードで討議し意見の一致が得られれば、陽子線治療の対象としている。

福井県の陽子線治療費は、照射回数が20回までは２４０万円、21～25回は２５０万円、26回以上は２６０万円であり、国立がんセンター東病院等の２８８万３０００円よりも低い金額に設定されている。福井県内の居住者（１年以上）には、25万円の減免措置がある。６月１日より先進医療の適応となり、がん保険の先進医療特約が利用できるようになった。

10月31日までに治療を開始した患者数は80

名で、その内訳は、前立腺がん25名、肺がん21名、肝細胞がん18名などである。福井県外からの患者数は17名で、石川県が6名ともっとも多く、愛知県、大阪府が各々3名、富山県が2名などとなっている。

12年3月までの1年目の予定治療患者数は110名と設定されているが、現在の状況が続けば今年度は目標を達成することができると考えている。ただし来年度以降、この年間目標患者数は順次増えていくことになっている。採算をとるための患者数は1年間に400名が必要と試算されており、この数まで患者数を増やしていくことが当面の目標となる。

患者数を増やすために
—適応範囲の拡大も重要な要素

10年の国勢調査によれば、兵庫県は人口560万人、静岡県が380万人に対し福井県は80万人で、石川県、富山県の人口を加えても310万人に達せず、静岡1県よりも少ない。がんの発生率が大きく変わらないことを考えると、福井県で陽子線治療の採算がとれる患者数を維持していくことは容易ではない。

診療開始から6ヵ月の時点では、福井県外からの患者数は20%程度であるが、今後、この割合を50%以上に高めていくことが必要と考えている。しかし、12年度には名古屋市内に新しい陽子線治療施設が開設される予定であり、愛知県や岐阜県等からの患者は期待できない。JR京都駅から特急に乗れば1時間20分でJR福井駅に到着する。これは富山駅—福井駅間の時間よりも短く、外来通院もできなくはない。北陸からばかりではなく、京都府や滋賀県など近畿圏からの患者を増やす努力が必要と考えられる。

陽子線治療の特徴の1つは、照射期間中に問題となるような急性の副作用がほとんどないので、原則として入院の必要がなく、通常の生活を続けながら外来でがん治療を受けられることである。しかし遠方のため通院が困難で、入院を希望しない患者や家族のことを考慮して、11年2月には、福井市旅館業協同組合およびあわら市観光協会と、陽子線がん治療のために宿泊を希望する患者や家族の方に宿泊・観光情報を提供するとともに、宿泊料金の割引や観光案内などの各種サービスを提供することを目的とした協定が締結された。

これまでに、福井市内のホテルに宿泊して陽子線治療を受けた患者は6名である。陽子線治療を受けながら、温泉につかって、永平寺や一乗谷の観光も楽しめるような宿泊プランの作成も検討している。

陽子線治療の最大の問題点の1つは、まだ健康保険の対象となっていないため患者負担が極めて高額となることである。そこで、民間のがん保険では、高額な先進医療費を支払う先進医療特約を追加できるタイプが増えている。福井県では、08年12月にアフラック等と協定を締結したのを最初に、先進医療特約のあるがん保険を取り扱っている保険会社23社と、陽子線がん治療施設が幅広く活用されるための活動ならびにがん検診の受診率向上に向けた啓発活動等を通じて、福井県が目指す「がん予防・治療日本一」の実現を図ることを目的として、相互に連携と協力を行っている。先進医療特約に加入していれば、健康保険の対象となっている通常のがん治療よりも患者の経済的な負担は小さくなると考えられる。また、福井県は、粒子線がん治療施設を導入または計画している11県4市の代表が集まる全国粒子線治療促進協議会の幹事を務めており、粒子線治療の健康保険への収載を目指し、厚生労働省などに要請活動を行うことを予定している。

陽子線治療はまだ一般にはなじみの薄い治療法であり、普及広報が重要である。そこで、依頼があれば担当者が出向き陽子線治療について分かりやすく紹介する「出前講座」を行っている。10年度には出前講座を125回、近県の主要病院での医療関係者向けの講演を15回など、合計約9400人に陽子線治療の説明を行い、11年度も引き続き実施している。

陽子線がん治療の適応範囲を拡大していくことも、患者数を増やすために重要な要素である。膵臓がんは、先行している兵庫県立粒子線医療センターを参考に試行し始めている。食道がんや進行肺がんに対する化学療法と陽子線治療の併用療法についても実施できるように準備を進めている。また、乳がんの陽子線治療を目指して、乳房の固定法の基礎的研究を行っている。若狭湾エネルギー研究センターでの陽子線がん治療臨床研究は終了したが、培養細胞や実験動物を用いて粒子線がん治療に関する基礎的研究が行えるように整備されており、陽子線治療のさらなる高度化を目指した共同研究を積極的に進めていく予定である。

また、採算性を改善するためには、必要な経費を厳密に見直して、より少ない経費で確

実に陽子線治療が実施できるようにする努力も必要である。

福井県立病院での陽子線がん治療
—患者から選ばれる治療法となることが大切

陽子線がん治療の採算性をよくするために最も重要なことは、陽子線治療が他の治療法よりも治療成績が高く、副作用が少ないという「エビデンス」を確立し、患者から選ばれるがん治療法となることである。福井県立病院という総合病院内に設置されていることを活かして、糖尿病、高血圧、心臓病といったがん以外の疾患に対しても適切な診療を並行して行うことで、全体として患者を癒す総合的な医療の実現を可能としている。

また、陽子線治療単独ばかりではなく、化学療法、手術療法など他のがん治療法とも適切に組み合わせて、個々の患者に対して最適ながん治療を行えるように検討し、治療成績の向上、治療対象の拡大を目指している。

人口の少ない地域で陽子線治療の採算がとれるような患者数を実現するのは容易ではないが、陽子線治療以外には適当な治療法がない患者も少なくはない。今後も、より多数の患者が陽子線治療を受けてよかったと実感できるように努力していきたいと考えている。

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山本和高（やまもと・かずたか）●50年兵庫県生まれ。76年京大医卒。91年福井医大放射線科助教授。98年若狭湾エネルギー研究センター粒子線医療研究室長。11年3月より福井県立病院陽子線がん治療センター長。

日本海側初の陽子線がん治療を開始
―福井県立病院陽子線がん治療センター

福井県立病院陽子線がん治療センター長
山本 和高(やまもと・かずたか)

3月から診療をスタート

福井県立病院陽子線がん治療センター(図1)は、平成23(2011)年3月7日に日本海側では最初の陽子線治療施設として診療を開始した。福井県立病院は、JR福井駅から車で5分程度の福井市内の便利な場所にある総合病院で、がん診療連携拠点病院に指定されており、がん医療センターが開設され、がん専門外来やがん専門病棟が設置されており、陽子線治療も含めて総合的かつ高度ながん治療を目指している。

図2は、陽子線がん治療センター1階の見取り図で、玄関を入ると受付があり、中央の待合ラウンジは吹き抜けになっており、右側に診察室、左側に治療室がある。治療装置は三菱電機製で、入射器は直線加速器(RFQ+DTL)で7MeVまで加速し、主加速器のシンクロトロンは周長約20m、陽子を235MeVまで加速し、最大平均ビーム電流は10nA、最大線量率は5Gy/minである。治療室は、水平固定照射室が1室、回転ガントリーを備えた治療室が2室の合計3室であるが、治療室3(図3)には、CT自動位置決めシステムと積層原体照射システムという新しい機能が付加されており、薬事法の認可を取得して平成24年からの臨床応用を予定している。2階には、CT、MRI、PET-CTの画像検査室と治療計画作成室が設置されている。

現在、放射線治療医4名、放射線技師7名、医学物理士3名、看護師2名等の職員で、頭頸部腫瘍、非小細胞肺がん、肝細胞がん、前立腺がん、転移性腫瘍を対象に作成した治療基準に基づいて陽子線治療を実施している。治療基準を満たしていないが、陽子線治療の可能性があると考えられる症例は、福井県立病院のキャンサー・ボードで討議し、了解が得られれば陽子線治療の対象としている。今後、食道がん、膵がん、乳がんなどにも、順次、陽子線治療基準を作成し、適応を拡げていく予定である。

保険会社や旅館組合などと連携

陽子線治療は、いまだ、保険診療の対象となっておらず、福井県では、照射回数に応じて240万円～260万円の治療費用が設定されている(福井県内の居住者には優遇制度あり)。そこで、福井県では、平成20年12月にアフラック等と協定を締結したのを最初に、先進医療に対する特約のあるがん保険などを取り扱っ

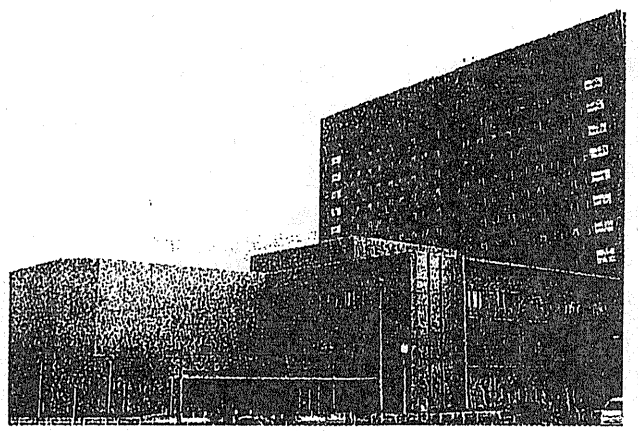

図1　福井県立病院陽子線がん治療センター外観(手前)。後は福井県立病院本棟

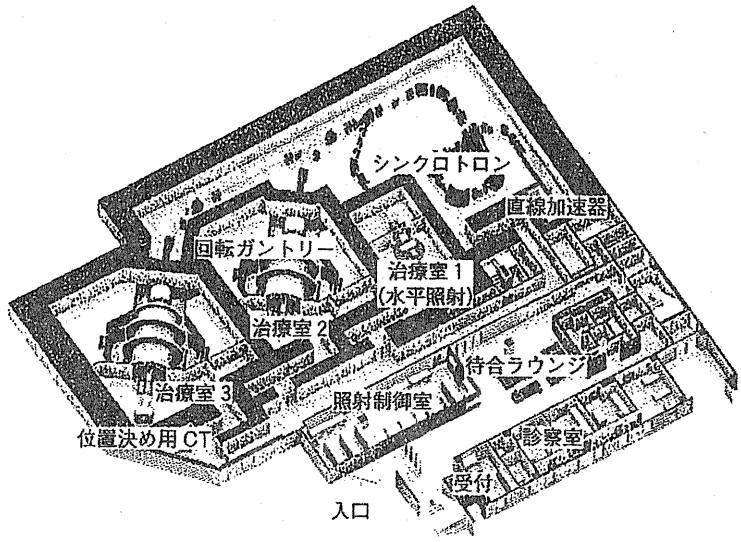

図2　陽子線がん治療センター1階見取り図

ている保険会社23社と、陽子線がん治療施設が幅広く活用されるための活動ならびにがん検診の受診率向上に向けた啓発活動等を通じて、福井県が目指す「がん予防・治療日本一」の実現を図ることを目的として、福井県と保険会社が相互に連携と協力を行っている。

また、陽子線治療はまだ一般にはなじみの薄い治療法であり、普及広報が重要である。そこで、依頼があれば担当者が出向いて、陽子線治療についてわかりやすく紹介する「出前講座」を行っている。平成22年度には出前講座を125回、近県の主要病院での医療関係者向けの講演を15回など、合計で約9400人に陽子線治療の説明を行い、平成23年度も続けている。

陽子線治療は、原則として入院の必要性が無いが、平成23年2月には、福井市旅館業協同組合およびあわら市観光協会と、陽子線がん治療のために宿泊を希望する患者や家族の方に宿泊・観光情報を提供するとともに、宿泊料金の割り引きや観光案内などの各種サービスを提供することを目的とした協定が締結された。

総合病院として特色を生かし治療対象拡大を目指す

福井県敦賀市にある若狭湾エネルギー研究センターでの陽子線がん治療臨床研究は終了したが、培養細胞や実験動物を用いて粒子線がん治療に関する基礎的研究が行えるように整備されており、陽子線治療のさらなる高度化を目指した共同研究を積極的に進めていく予定である。

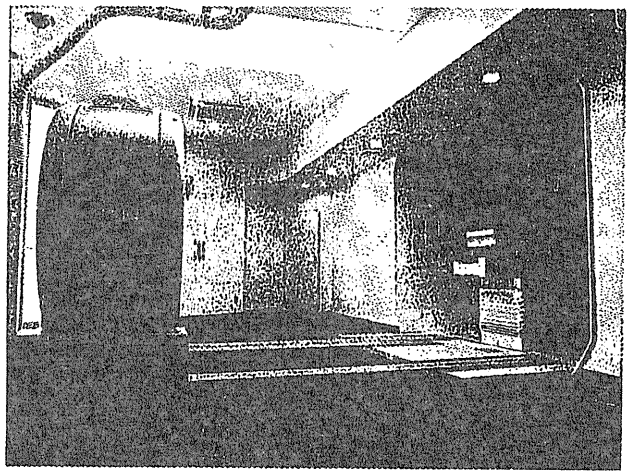

図3　治療室3。左側にCT自動位置決めのためのCTが設置されている

県立病院という総合病院内に設置されていることを活かして、糖尿病、高血圧、心臓病といったがん以外の疾患に対しても適切な診療を並行して行うことで、全体として患者を癒す総合的な医療の実現を可能としている。また、陽子線治療単独ばかりではなく、化学療法、手術療法など他のがん治療法とも適切に組み合わせて、個々の患者に対して最適ながん治療を行えるように検討し、治療成績の向上、治療対象の拡大を目指している。

陽子線治療の適応となる各疾患の治療基準や、出前講座等についての詳細は福井県立病院陽子線がん治療センターのホームページ(http://info.pref.fukui.jp/imu/fph/youshisen/index.html)をご覧ください。

Original article

Risk factors for survival and local recurrence after particle radiotherapy for single small hepatocellular carcinoma

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Background: Particle radiotherapy is a novel treatment for malignant tumours. The present study aimed to evaluate risk factors for overall survival and local control after particle radiotherapy of single small hepatocellular carcinoma (HCC), and to identify suitable candidates for this treatment.

Methods: All patients with a single HCC smaller than 5 cm in diameter treated by particle radiotherapy between 2001 and 2008 were identified retrospectively from a prospectively collected database. Clinical outcomes and prognostic factors were analysed.

Results: A total of 150 patients were included. Five-year overall survival and local control rates were 50·9 and 92·3 per cent respectively. Multivariable analysis revealed that several factors, including age and Child–Pugh classification, significantly influenced overall survival. Proximity to the digestive tract and Child–Pugh classification were independent risk factors for local recurrence. Other tumour factors including size, gross classification, previous treatment, macroscopic vascular invasion, and tumour location in relation to the diaphragm and large vessels did not influence local control rate.

Conclusion: Particle radiotherapy seems safe and effective, and may be a novel treatment for small HCC. Recurrences are more frequent when the tumour is located close to the gut.

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Introduction

Hepatocellular carcinoma (HCC) is one of the most common malignancies worldwide[1]. Hepatectomy and liver transplantation are considered to be the most reliable treatments for HCC, but benefit only approximately 15 per cent of patients[2]. Local ablative therapies, such as radiofrequency ablation (RFA), are commonly used to treat unresectable liver tumours, but may lead to increased local recurrence rates[3–5]. Tumour size and perivascular tumour location are significant risk factors for local recurrence after RFA[4,5]. Patients not eligible for local ablative therapy are usually treated with non-curative modalities, such as transarterial chemoembolization (TACE) or systemic chemotherapy.

Recent improvements in photon radiotherapy, such as conformal three-dimensional planning, intensity-modulated radiotherapy and breathing motion management strategies, have made it possible to irradiate smaller targets in the liver with curative intent. However, these highly computer-assisted irradiation techniques using photon beams have still achieved only limited efficacy in treating large and centrally situated liver tumours[6–8].

Particle beams consisting of protons and carbon ions offer improved dose distribution compared with photons, and therefore enable dose escalation within the tumour while sparing normal tissues. The similar effectiveness of proton and carbon ion radiotherapy has already been proven in several clinical reports[9–13]. Consequently particle radiotherapy has become a realistic treatment option for HCC. However, the best therapeutic targets and the limitations of particle radiotherapy for HCC still remain to be elucidated. The aim of the present study was to identify risk factors for overall survival and local control following particle radiotherapy of a single small HCC.

Methods

An institutional database containing prospectively collected data on patients treated at the Hyogo Ion Beam Medical

Centre was studied retrospectively. Patients who had uncontrolled ascites, multiple tumours and/or tumours larger than 5 cm were not eligible for inclusion. All patients had HCC diagnosed either histologically or clinically based on contrast-enhanced computed tomography (CT) and/or magnetic resonance imaging (MRI), and raised levels of α-fetoprotein (AFP) and/or proteins induced by vitamin K absence or antagonist II (PIVKAII). This group included patients ineligible for hepatectomy owing to poor liver function (indocyanine green retention rate at 15 min exceeding 30 per cent) and/or poor performance status, as well as those who deliberately chose to undergo particle radiotherapy as a less invasive curative treatment for HCC. Some of these patients had undergone previous treatments comprising combinations of either surgery, TACE or local ablative therapy. Data were analysed retrospectively with regard to overall survival, local tumour control and treatment-related toxicity. The present study was conducted according to the Helsinki Declaration, and written informed consent was obtained from all patients.

Abdominal CT, MRI, ultrasonography, chest CT and bone scintigraphy were carried out to determine the clinical stage before treatment. All patients had a complete blood count, a biochemical profile including total protein, albumin, total cholesterol, electrolytes, kidney and liver function tests, and serological testing for hepatitis B surface antigen and antihepatitis C antibody. Serum AFP and PIVKAII levels were also measured before and after treatment.

Baseline patient and tumour variables were analysed. Tumour size was classified as either 30 mm or less, or over 30 mm (but less than 50 mm) in largest dimension. Tumours were divided into four gross types according to the rules of the Liver Cancer Study Group of Japan[14]: single nodular type, single nodular type with extranodular growth, confluent multinodular type and infiltrative type. As single nodular tumours have a better prognosis than other types[15], tumours were further categorized as either single nodular or non-single nodular type. Macroscopic vascular invasion was defined as gross tumour invasion into the portal or hepatic veins on pretreatment imaging. Tumour location was also classified based on proximity to the digestive tract (within 10 mm, 10 mm or more), diaphragm (within 10 mm, 10 mm or more), inferior vena cava (IVC) (attached, not attached) and main portal trunk (attached, not attached).

Protocol and treatment planning

The prescribed dose was calculated for the centre of the planning target volume (PTV) and expressed in gray (Gy) equivalents (GyE = proton or carbon physical dose (in Gy) × relative biological effectiveness). Four protocols for proton radiotherapy (52·8–76 GyE in 4–20 fractions using 150-, 190-, 210- or 230-MeV proton beams) and two protocols for carbon ion radiotherapy (52·8 GyE in 4–8 fractions using 250- or 320-MeV carbon ion beams) were employed in the present study. From May to October 2001 and from April 2003 to March 2005, only proton radiotherapy was available. From February to June 2002, only carbon ion radiotherapy was available. After April 2005, treatment plans were made for both proton and carbon ion radiotherapy to allow selection of the better beam[16]. From November 2001 to January 2002, and from July 2002 to March 2003, treatments were not performed because of the licensing procedure. The dose distribution in a single beam appears to be better in carbon ion beams than in proton beams[17]. However, in terms of beam arrangement, carbon ions are emitted from three fixed ports, whereas a 360° rotating gantry can be used for protons. The high positioning accuracy achieved by irradiating patients in a supine position is therefore an advantage of proton radiotherapy.

Radiation treatments were designed with the use of a CT-based three-dimensional treatment planning system (FOCUS-M; CMS Japan, Tokyo, and Mitsubishi Electric, Kobe, Japan). In brief, the patient was immobilized with a custom-made thermoplastic immobilization cast in the supine or prone position, depending on the tumour location. CT slice thickness was 2 mm and MRI slice thickness 5 mm. CT images were obtained at expiration using a respiratory gating system. Target volumes and organs at risk of irradiation, such as the liver and intestine, were delineated on CT–MRI fusion images. Treatment planning was defined in terms of the clinical target volume (CTV). CTV = gross tumour volume + 5 mm (in all directions), PTV = CTV + 5 mm (in all directions). In addition, a further margin of 5–10 mm was included in the caudal axis to compensate for respiration-induced hepatic movements. Dose–volume histograms were made for all patients to evaluate the risk of radiation-induced complications. All treatment plans were established and modified according to the tolerance limits of the exposure doses of each organ.

Doses were calculated based on the pencil beam algorithm. The beam parameters, including energy level, width of the spread-out Bragg peak, and degrader thickness were selected adequately with FOCUS-M.

New symptoms or clinical findings developing within 90 days of the initiation of particle radiotherapy were defined as acute radiation toxicity, and later problems as late toxicity. Acute and late toxicities were graded by severity of

adverse event according to the National Institute Common Terminology Criteria for Adverse Events (version 2.0): grade 1, mild; grade 2, moderate; grade 3, severe; and grade 4, life-threatening or disabling[18].

Follow-up and evaluation criteria

Follow-up consisted of blood tests and monitoring of tumour markers in outpatients; dynamic CT or MRI was performed every 3 months for 3 years after treatment, and every 6 months thereafter.

As HCCs, even after a complete response, tend to persist for a long period after completion of particle radiotherapy[12], local recurrence was defined as either growth of an irradiated tumour or the appearance of new tumours within the PTV, based on previous criteria[9,10,12].

Statistical analysis

Overall survival and local control rates were calculated using Kaplan–Meier methodology. Eight patient variables (age, sex, positive viral marker, performance status, Child–Pugh classification, serum AFP level, PIVKAII level and source of beam) (*Table 1*) and eight tumour features (tumour size, gross classification, previous treatment of target tumour, macroscopic vascular invasion, proximity to the digestive tract, proximity to the diaphragm, proximity to the IVC and proximity to the main portal trunk) (*Table 2*) were investigated as prognostic factors for overall survival and local control. The statistical significance of differences in both overall survival and local control rates was examined using the log rank test in univariable analysis. $P < 0{\cdot}050$ was considered statistically significant, and variables with $P < 0{\cdot}100$ were included in multivariable analysis using Cox proportional hazards model. Statistical analyses were performed using SPSS® version 17.0 software (SPSS, Chicago, Illinois, USA).

Results

Of 339 consecutive patients treated between May 2001 and December 2008, 150 who had a single tumour measuring less than 5 cm in diameter were eligible for inclusion in the study. Eighty-six (57·3 per cent) of the 150 patients had no history of tumour treatment before particle radiotherapy. The remaining 64 had received treatment to the target tumour previously. Two of the 64 patients had local recurrence after hepatectomy and 23 developed local recurrence after local ablative therapy. In addition, 56 of these 64 patients had undergone TACE before particle radiotherapy.

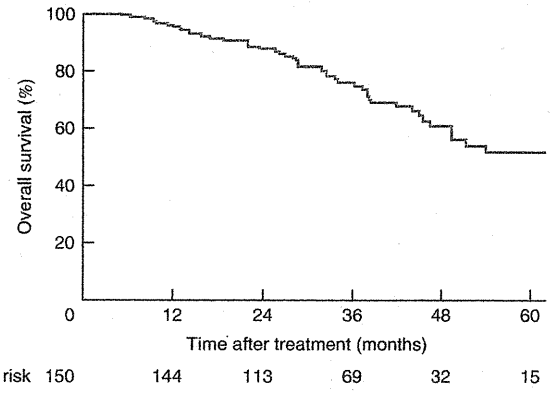

Fig. 1 Overall survival rate among 150 patients treated with particle radiotherapy for a single small hepatocellular carcinoma

Prognostic factors for overall survival

Overall survival rates for all patients at 3 and 5 years were 75·7 and 50·9 per cent respectively (*Fig. 1*). Age, performance status and Child–Pugh classification were identified as significant prognostic factors for overall survival rate in univariable analysis (*Tables 1* and *2*). Multivariable analysis showed that age and Child–Pugh classification were independent factors that significantly affected overall survival (*Table 3*).

Prognostic factors for local control

The cumulative local control rates for all tumours at 3 and 5 years were both 92·3 per cent (*Fig. S1*, supporting information). Univariable analysis showed that sex, performance status, Child–Pugh classification and proximity to the digestive tract significantly affected local control rates (*Tables 1* and *2*). Other tumour factors, including size, gross classification, history of previous treatment, macroscopic vascular invasion and tumour location (proximity to the diaphragm, IVC and main portal trunk) did not affect local control rates. Child–Pugh classification and proximity to the digestive tract were the only independent factors for local recurrence in multivariable analysis (*Table 3; Fig. S2*, supporting information).

Toxicity

All patients tolerated the treatment and completed the planned treatment protocol. A total of 127 patients

Table 1 Univariable analysis of factors related to patient characteristics

		5-year overall survival		5-year local control	
	No. of patients	Rate (%)*	Univariable *P*†	Rate (%)*	Univariable *P*†
Age (years)			0·049		0·696
< 70	69 (46·0)	58·0		93·7	
≥ 70	81 (54·0)	43·2		91·0	
Sex			0·265		0·037
M	115 (76·7)	52·6		95·0	
F	35 (23·3)	45·8		83·9	
Positive viral marker			0·715		0·753
Hepatitis B virus	23 (15·3)	47·9		94·1	
Hepatitis C virus	104 (69·3)	50·0		91·4	
None	23 (15·3)	68·2		95·2	
Performance status			0·036		0·023
0	118 (78·7)	57·0		95·2	
1 or 2	32 (21·3)	29·3		82·1	
Child–Pugh classification			< 0·001		0·007
A	125 (83·3)	59·8		94·6	
B	25 (16·7)	14·6		77·1	
Serum AFP (ng/ml)			0·514		0·934
< 100	118 (78·7)	51·0		92·4	
≥ 100	32 (21·3)	50·3		92·0	
Serum PIVKAII (units/ml)			0·090		0·823
< 100	97 (64·7)	56·2		91·9	
≥ 100	53 (35·3)	38·2		93·4	
Source of beam			0·389		0·972
Proton	105 (70·0)	49·1		92·5	
Carbon	45 (30·0)	68·0		91·9	

Values in parentheses are percentages. AFP, α-fetoprotein; PIVKAII, proteins induced by vitamin K absence or antagonist II. *Kaplan–Meier analysis; †log rank test.

Table 2 Univariable analysis of tumour factors

		5-year overall survival		5-year local control	
	No. of patients	Rate (%)*	Univariable *P*†	Rate (%)*	Univariable *P*†
Tumour size (mm)			0·612		0·924
≤ 30	89 (59·3)	50·0		92·2	
> 30, ≤ 50	61 (40·7)	52·5		92·8	
Gross classification			0·178		0·118
Single nodular type	91 (60·7)	52·7		95·0	
Non-single type	59 (39·3)	48·1		87·9	
Previous treatment of tumour			0·328		0·591
Yes	64 (42·7)	44·5		90·9	
No	86 (57·3)	56·0		93·3	
Macroscopic vascular invasion			0·998		0·729
Yes	10 (6·7)	70·0		88·9	
No	140 (93·3)	49·9		92·7	
Proximity to digestive tract (mm)			0·236		0·009
≤ 10	20 (13·3)	42·2		77·8	
> 10	130 (86·7)	52·5		94·8	
Proximity to diaphragm (mm)			0·941		0·753
≤ 10	50 (33·3)	51·5		93·4	
> 10	100 (66·7)	51·3		91·8	
Proximity to IVC			0·761		0·593
Attached	33 (22·0)	61·8		88·9	
Not attached	117 (78·0)	48·7		93·3	
Proximity to main portal trunk			0·649		0·295
Attached	15 (10·0)	56·7		84·4	
Not attached	135 (90·0)	50·1		93·2	

Values in parentheses are percentages. IVC, inferior vena cava. *Kaplan–Meier analysis; †log rank test.

Table 3 Independent risk factors for overall survival and local control identified by multivariable analysis

	Standard error	χ^2	Hazard ratio	Multivariable *P**
Overall survival				
Age > 70 years	0·322	8·25	2·52 (1·34, 4·74)	0·004
Performance status 1 or 2	0·332	3·68	1·89 (0·99, 3·63)	0·055
Child–Pugh classification B	0·336	31·54	6·59 (3·41, 12·72)	< 0·001
Serum PIVKAII ≥ 100 units/ml	0·316	2·94	1·72 (0·92, 3·19)	0·086
Local control				
Female sex	0·649	1·42	2·17 (0·61, 7·75)	0·232
Performance status 1 or 2	0·637	3·57	3·33 (0·96, 11·63)	0·058
Child–Pugh classification B	0·670	3·85	3·72 (1·00, 13·85)	0·049
Proximity to digestive tract ≤ 10 mm	0·663	5·25	4·57 (1·25, 16·76)	0·021

Values in parentheses are 95 per cent confidence intervals. PIVKAII, proteins induced by vitamin K absence or antagonist II. *Cox proportional hazards regression model.

developed acute toxicity, but this was grade 2 or less in the majority. Grade 3 or higher toxicity was observed in eight patients, but always resolved within 2 weeks and no patient discontinued treatment owing to acute toxicity. With regard to late toxicity, grade 3 dermatitis was noted in one patient; there was no grade 4 toxicity. No patient died from treatment-related toxicity.

Exposure of a portion of non-cancerous liver to particle radiotherapy induced hepatitis and the gradual development of dense fibrosis, resulting in almost complete atrophy.

Discussion

The present study has shown that particle radiotherapy for small HCC is feasible and safe, with overall survival and local control rates similar to those of other local therapies. Proximity to the digestive tract was identified as a significant risk factor for local recurrence after particle radiotherapy. This strongly suggests that marginal parts of tumours close to the digestive tract had received an insufficient dose. Two factors may contribute to this finding. First, a safety margin around the radiation field cannot be ensured for tumours close to the bowel owing to unavoidable respiratory movements. Second, most tumours near the gut are situated on the inferior surface of the liver. As a result, dose centralization of the particle beams is hindered more prominently by the patient's normal respiratory movements in this region than in other areas of the liver. These factors may reduce the safety margin against the dosimetric and geometric uncertainties of particle beams, and could lead to an increase in local recurrence rates. Each local therapy of HCC has inherent limitations regarding the tumour location[4,19]. Tumour location on the inferior surface of the liver, close to the digestive tract, is probably the Achilles heel of particle radiotherapy for HCC. To overcome this limitation, a spacer between the tumour and digestive tract may be inserted before particle radiotherapy[20,21].

Tumour size greater than 3 cm is a significant risk factor for local recurrence after local ablative therapies, such as RFA[5,22]. In contrast, tumour size over 3 cm (but smaller than 5 cm) had no significant effect on the local control rate in the present study. This suggests that, for tumours up to 5 cm in diameter, particle radiotherapy is effective in achieving local control, irrespective of tumour size. This may be a distinct advantage over existing local ablative therapies.

Macroscopic vascular invasion and three other factors related to tumour location (proximity to the diaphragm, IVC and main portal trunk) had no significant influence on the local control rate after particle radiotherapy. This also differs from findings for other local ablative therapies. The application of local ablative therapies is contraindicated for tumours with macroscopic vascular invasion[5]. Furthermore, proximity to major vessels such as the IVC and/or main portal trunk is associated with an increased local recurrence rate after RFA, as a result of the heat-sink effect[4,5]. Others have shown proximity to the diaphragm to be another factor for local recurrence after percutaneous RFA[23,24]. Hepatectomy is felt to be inappropriate in the treatment of centrally situated tumours adjacent to the IVC and/or the main portal trunk in patients with liver cirrhosis[19]. In the present study, however, none of these factors reduced the efficacy of particle radiotherapy in controlling local growth. In particular, particle radiotherapy was equally effective and safe in treating tumours adjacent to the porta hepatis, confirming previous findings[25]. Based on these results, particle radiotherapy would be an attractive therapeutic option for tumours that are not suitable for currently available local therapies owing to size, location and/or vascular invasion.

Child–Pugh classification was the only independent patient factor with a significant influence on overall survival and local control based on both univariable and multivariable analyses. Several other studies have reported that severe fibrosis or cirrhosis has an independent effect on overall survival rates after curative resection[26,27]. Likewise, poor overall survival rates in the present study were strongly associated with pretreatment liver function (Child–Pugh B), regardless of complete remission of the primary tumour. As regards the poor local control rate in patients with Child–Pugh grade B disease, one possible explanation is that liver cirrhosis is associated with *de novo* carcinogenesis and multicentric recurrence may occur adjacent to the target tumour in cirrhotic liver. This type of multicentric recurrence might therefore be considered to represent local recurrence.

Particle beams, such as proton and carbon ion beams, show an increase in energy deposition with penetration depth up to a sharp maximum at the end of their range, to form the so-called Bragg peak. Almost no dose is deposited in normal tissue beyond the Bragg peak. The particle range is determined by the energy of the incoming particles. Favourable dose distributions with a steep dose fall-off at the field borders, and therefore a more precise dose escalation, can be achieved with these beams in comparison with photon beams. Therefore, dose escalation can probably be performed without inducing toxicity in the surrounding normal tissues.

Acute and late toxicities during treatment were all transient, easily manageable and acceptable in the present series. Previous studies have also shown that particle radiotherapy is safe and less invasive than other treatment modalities for HCC[9,11]. However, dense fibrosis developed in non-cancerous liver that had been exposed to particle radiotherapy, resulting in almost complete atrophy. Therefore, particle radiotherapy should be applied judiciously in patients whose liver function has deteriorated.

At present, the candidates best suited for particle radiotherapy are those with tumours situated more than 10 mm from the digestive tract, in whom other local therapies are contraindicated owing to tumour size, location or vascular invasion, and those with recurrence after hepatectomy, local ablative therapy and TACE.

This study has three limitations: different treatment protocols for proton and carbon ion radiotherapy were used during the study interval; the data were analysed retrospectively; and no direct comparison with other local therapies was made. Although further investigation is required, the present data can serve as a basis for selecting particle radiotherapy as a local treatment for HCC. A comparison with other therapies, such as internal radiation with yttrium-90 microspheres, would be interesting and prospective comparison with resection might be justified.

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Supporting Inofmration may be found in the online version of this article

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Supporting information

Additional supporting information may be found in the online version of this article:

Fig. S1 Local control rate among 150 patients treated with particle radiotherapy for a single small hepatocellular carcinoma (Word document)

Fig. S2 Local control rate among 150 patients treated with particle radiotherapy for a single small hepatocellular carcinoma stratified according **a** Child–Pugh classification and **b** proximity to the digestive tract (Word document)

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Original Article

Clinical Results and Risk Factors of Proton and Carbon Ion Therapy for Hepatocellular Carcinoma

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BACKGROUND: The objective of this study was to evaluate the clinical outcome of proton and carbon ion therapy for hepatocellular carcinoma (HCC). **METHODS:** In total, 343 consecutive patients with 386 tumors, including 242 patients (with 278 tumors) who received proton therapy and 101 patients (with 108 tumors) who received carbon ion therapy, were treated on 8 different protocols of proton therapy (52.8-84.0 gray equivalents [GyE] in 4-38 fractions) and on 4 different protocols of carbon ion therapy (52.8-76.0 GyE in 4-20 fractions). **RESULTS:** The 5-year local control and overall survival rates for all patients were 90.8% and 38.2%, respectively. Regarding proton and carbon ion therapy, the 5-year local control rates were 90.2% and 93%, respectively, and the 5-year overall survival rates were 38% and 36.3%, respectively. These rates did not differ significantly between the 2 therapies. Univariate analysis identified tumor size as an independent risk factor for local recurrence in proton therapy, carbon ion therapy, and in all patients. Multivariate analysis identified tumor size as the only independent risk factor for local recurrence in proton therapy and in all patients. Child-Pugh classification was the only independent risk factor for overall survival in proton therapy, in carbon ion therapy, and in all patients according to both univariate and multivariate analyses. No patients died of treatment-related toxicities. **CONCLUSIONS:** Proton and carbon ion therapies for HCC were comparable in terms of local control and overall survival rates. These therapies may represent innovative alternatives to conventional local therapies for HCC. ***Cancer* 2011;117:4890–904.** © *2011 American Cancer Society.*

KEYWORDS: hepatocellular carcinoma, particle therapy, proton therapy, carbon ion therapy, local recurrence.

Hepatocellular carcinoma (HCC) is the fifth leading cause of cancer death worldwide, and the majority of patients with HCC reside in Asian countries.[1,2] HCC is well suited to local therapy, because it has a tendency to stay within the liver, and distant metastasis generally occurs late. This implies that curative local therapy, as represented by hepatectomy and liver transplantation, has a great impact on the disease course and also offers the best chance of long-term survival for patients with HCC.[3,4] However, only 5% to 40% of patients with HCC are amenable to a hepatectomy because of either advanced tumors or coexisting cirrhosis,[5,6] and a shortage of liver grafts limits the applicability of liver transplantation. Although local ablative therapies, such as radiofrequency ablation (RFA), recently have gained widespread clinical acceptance, there is growing evidence of a high local recurrence rate after RFA that reaches up to 36%.[7,8] In addition, local ablative therapies also are unsuitable for patients who have bleeding tendencies, unfavorable anatomic tumor locations, or large tumors.[8,9] Patients who are not eligible for local ablative therapies usually receive noncurative modalities, such as transarterial chemoembolization (TACE) or systemic chemotherapy.

Radiotherapy also is a local therapy but historically has played a limited role in the treatment of HCC, because the hepatic tolerance dose is lower than the tumoricidal dose, especially when liver function is impaired by chronic liver disease.[10-12] Particle beams, such as proton and carbon ion beams, have demonstrated an increase in energy deposition with a penetration depth up to a sharp maximum at the end of their range: the so-called Bragg peak phenomenon.[13] Therefore, higher tumor doses can be delivered without increasing toxicity to the surrounding noncancerous tissues and organs. Particle therapy results for HCC have been reported in several case series, all of which have reported good overall survival and encouraging local control rates.[14-19] However, most of those studies were conducted at proton treatment centers, and few

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Table 1. Patient Characteristics

Characteristic	No. of Patients (%)		
	Proton Therapy, n=242	Carbon Ion Therapy, n=101	All Patients, n=343
Age, y			
<70	115 (48)	55 (54)	170 (50)
≥70	127 (52)	46 (46)	173 (50)
Sex			
Men	182 (75)	73 (72)	255 (74)
Women	60 (25)	28 (28)	88 (26)
Positive viral marker			
Hepatitis B virus	27 (11)	19 (19)	46 (13)
Hepatitis C virus	159 (66)	60 (59)	219 (64)
None	54 (22)	21 (21)	75 (22)
Both	2 (1)	1 (1)	3 (1)
Performance status			
0	172 (71)	73 (72)	245 (71)
1	57 (24)	18 (18)	75 (22)
2	10 (4)	9 (9)	19 (6)
3	3 (1)	1 (1)	4 (1)
Child-Pugh classification			
A	184 (76)	78 (77)	262 (76)
B	55 (23)	20 (20)	75 (22)
C	3 (1)	3 (3)	6 (2)
BCLC stage			
0	9 (4)	9 (9)	18 (5)
A	82 (34)	36 (36)	118 (34)
B	32 (13)	15 (15)	47 (14)
C	113 (47)	37 (36)	150 (44)
D	6 (2)	4 (4)	10 (3)
Recommended treatment according to BCLC stage			
Resection: Operable group	49 (20)	29 (29)	78 (23)
Others: Inoperable group	193 (80)	72 (71)	265 (77)
No. of tumors			
Single	213 (88)	81 (80)	294 (86)
Multiple	29 (12)	20 (20)	49 (14)

Abbreviations: BCLC, Barcelona Clinic Liver Cancer.

studies have reported results of carbon ion therapy for HCC. To our knowledge, no reports have focused on the differences in treatment results between the 2 types of particle beams.

The Hyogo Ion Beam Medical Center (HIBMC) is the only facility in the world that provides both proton and carbon ion therapies.[20] In the current study, we analyzed the efficacy and safety of proton and carbon ion therapy for HCC at the HIBMC.

MATERIALS AND METHODS

Patient and Tumor Characteristics

The current study was conducted according to the Helsinki Declaration, and written informed consent was obtained from all patients. From May 2001 to January 2009, 343 consecutive patients with 400 HCCs were treated at the HIBMC (excluding 6 patients who discontinued treatment). Patients who met the following conditions were ineligible for treatment: 1) uncontrolled ascites and 2) tumors that measured >15 cm in greatest dimension (the upper limit of the irradiation field). No patients were lost to follow-up, although we could not evaluate the post-treatment imaging findings from 12 patients with 14 tumors. Thus, overall survival rates were determined for all 343 patients, and local control rates were determined for 386 tumors. In total, 242 patients with 278 tumors received proton therapy, and 101 patients with 108 tumors received carbon ion therapy. For all patients,