Three-Dimensional Conformal Radiation Therapy and Periodic Irradiation with the Deep Insipration Breath-Hold Technique for Hepatocellular Carcinoma

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Abstract

Nine cases of primary hepatocellular carcinoma were treated with 3D-conformal radiation therapy using computerized planning system. This technique permits the precise delivery of a high dose of radiation to the target while sparing most of the normal liver tissue. In order to decrease the effect of organ movement related to respiration, periodical irradiation was combined with the deep inspiration breath-hold technique. The radiation dose was equivalent to conventional radiation with a total dose of 50-70 Gy with 2 Gy, 5 times a week. Irradiation was given in 1-10 fractions which encompassed the target with 90 per cent isodose line. The patients tolerated the treatment procedure well without any complications inherent to the technique. The tumors were decreased in size, the pain symptom and abdominal discomfort were relieved for 3-20 months. This technique is an effective and safe treatment for palliation in hepatocellular carcinoma especially in locally advanced stages with large or multiple lesions. However, long term follow-up should be done to evaluate the late radiation effect and clinical outcome.

Key word : Hepatocellular Carcinoma, Three-Dimentional Conformal Radiationa Therpy, Periodic Irradiation with Deep Inspiration Breath-Hold Technique

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Hepatocellular carcinoma (HCC) is one of the most common cancers in Thailand. The optimal treatment for advanced HCC has not yet been established. The prognosis of untreated HCC is generally poor. Currently, the only treatment capable of significantly prolonging survival in patients with a solitary lesion of hepatocellular carcinoma is complete resection. However, the overall result is still poor even in hepatectomy patients because of the high incidence of recurrence and low rate of survival[1,2]. For these patients, palliative treatment to prolong survival and improve the patient's quality of life is considered to be meaningful[3,4]. Conventional radiation therapy for primary hepatoma has been limited by the ability to deliver a sufficient dose to the tumor without inducing fatal liver toxicity especially in patients with poor liver function and minimal normal liver reserve. Radiation hepatitis can occur with whole liver irradiation dose in the range of 24-30 Gy depending on the time dose fraction scheme[5-7].

The improvement of radiation techniques, such as stereotactic radiosurgery and radiotherapy, are accepted as being as effective as a loco-regional treatment modality as surgery. The application of 3D-conformal radiation therapy to liver cancer has allowed higher doses to be delivered safely with encouraging responses and improving survival rates [8]. A three dimensional treatment planning system and conformal radiotherapy facilitates treatment by providing a mechanism for conforming the high-dose treatment volume to the target volume, thus minimizing the dose to adjacent uninvolved normal structures. This process involves graphic reconstruction of 3-dimentional images from multiple cross-sectional images, beam-eye-views display, rapid dose calculations and dose display, and the interactive modification of beam parameters to allow target dose coverage and exclude uninvolved tissue. However, the movement of intrathoracic and intraabdominal targets during treatment is still a major problem for conforming radiation technique. Periodical irradiation with the corresponding patient's respiratory phase technique for lung metastasis was reported. Thus, the deep inspiration breath-hold technique was used in primary hepatocellular carcinoma in this study.

MATERIAL AND METHOD

Retrospective-reviewed cases of advanced, inoperable hepatocellular carcinoma treated with 3 Dimensional Conformal Radiation Therapy (3D-CRT) from September 1996 to March 2000 in Srisiam Hospital are presented. Nine cases of advanced hepatoma were treated with the deep inspiration breath-hold technique, 7 males and 2 females with an age range of 30-75 years old. The most common symptoms were pain and weight loss.

The patients were positioned and immobilized on the CT-scanner couch with the plastic markers placed in the midline and lateral sides (flank) of the body along the laser beam. The position was set with these markers throughout the treatment procedure. Axial CT images, with 0.5 cm slice thickness cut through the whole liver were obtained during full inspiration. The CT images were transferred directly to the computerized treatment planning system (focus 3D-RTP). The external contour, normal critical organ and clinical target volume (CTV) were outlined. The planning target volume (PTV) was defined as 0.5 cm margin. The treatment plannings were done according to the shape of the tumor and critical organs nearby. Multiple arc rotation beams and static beams of different couch angles were used. The ninety-per cent isodose line was chosen to encompass the target while sparing most of the normal liver tissue. (Fig. 1) After the treatment plan was approved, the treatment isocenter was transferred to the patient's surface. The CT image at isocenter level was done to confirm the treatment

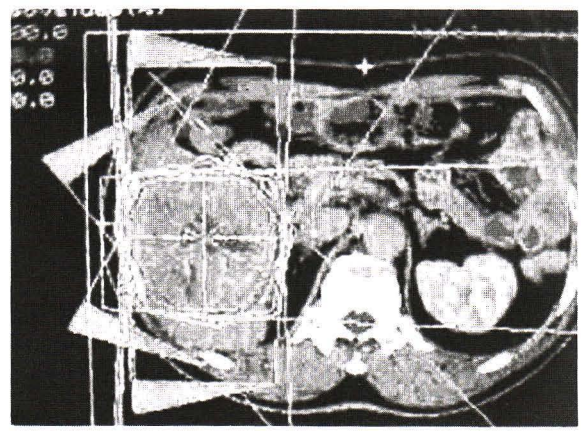


Fig. 1. The treatment planning shows multiple beams with block and dose cover only of the tumor with sparing the normal liver.

Table 1. Patients and tumor characteristics, radiation dose and response.

Sex	Age	Size (cm)	Lesion(s)	Equivalent dose	Result
Male	51	3 x 3	Single	66 Gy	CR
Male	74	12 x 10	Multiple	66 Gy	PR
		5 x 5.2		50 Gy	PR
Male	36	20 x 15	Multiple	50 Gy	PR
Female	64	7.5 x 5	Single	60 Gy	PR
		5 x 7		60 Gy	PR
Male	30	14 x 7	Multiple	70 Gy	PR
		5.5 x 6		70 Gy	PR
		5.5 x 2.5		60 Gy	PR
Male	57	5.5 x 3.5	Multiple	60 Gy	PR
		2.5 x 3		65 Gy	PR
Female	75	15 x 13	Single	60 Gy	CR
Male	57	7 x 8.5	Multiple	70 Gy	PR
Male	62	5.5 x 7.5	Multiple	70 Gy	CR
		6 x 6.8		70 Gy	PR
		6.5 x 2		20 Gy	PR
		6 x 3.5		60 Gy	PR

plan and the patient's position while the patient was set up in the same position.

To correct the effect of organ movement from breathing, irradiation was given only during the period of full inspiration. The patients were trained to keep their full inspiration as long as they could and only 80 per cent of the duration when they could hold their breath was used as the period of irradiation. So, each treatment had to be divided into small multiple sessions related to the period that the patients could hold their breath. The confirmation of isocenter localization in the target was done by CT scan in the breath holding process.

This technique of radiation can be done only with good cooperation of the patients. The process of treatment was clearly explained to the patient. In case of inability to further the breath holding, the patients were asked to raise their hand so the technician could detect the motion *via* the closed-circuit television, and the irradiation was paused. In the treatment room, the patients were set up and immobilized by the same position as for the CT scanning. At least two radiation technologists were needed for this treatment procedure. The first one worked on the treatment machine while the other controlled the patient's respiration during treatment through the intercom, and observed the patient from the closed-circuit television. In the early phase, the authors prescribed one or two fractions of radiation therapy of 20 Gy which is equivalent to 70 Gy with 2 Gy per fraction, 5 fractions a week by TDF calculation. For the later period, we increased the number of fractions to improve the biological effect to the tumor and normal tissue.

RESULT

In these nine patients, the tumor mass size was 3-20 cm, 3 cases had a single lesion and 6 cases had multiple lesions. Seventeen sessions of (3D-CRT) were given. One to ten fractions in each session were used with a total dose of 50-70 Gy equivalent for each lesion. The highest number of sessions was four in one patient. The patient's characteristics and treatment are shown in Table 1.

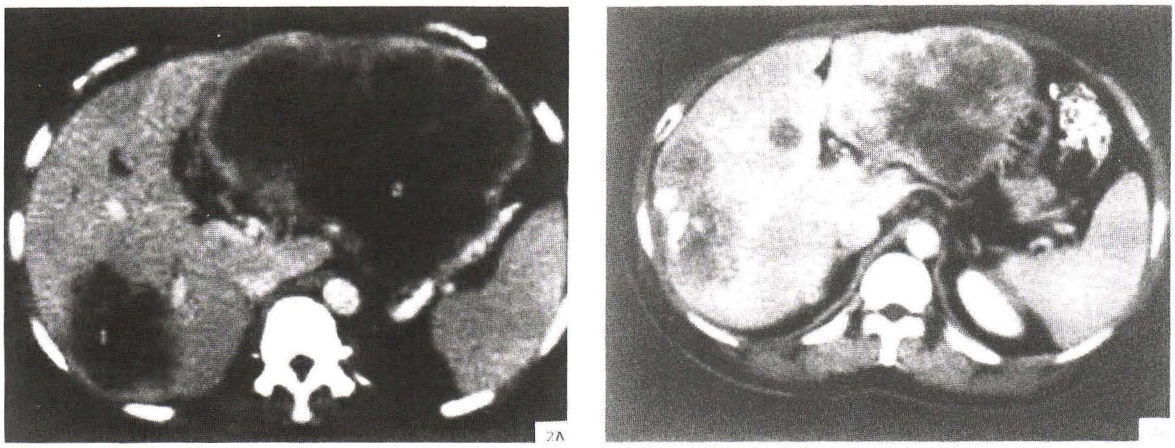
The subjective response to treatment was interpreted by CT-images as

1. Complete response (CR) : The tumor disappeared from the follow-up CT images.

2. Partial response (PR) : The tumor showed some degree of decrease in size in CT-images.

3. No response (NR) : The tumor showed no change in size or progression.

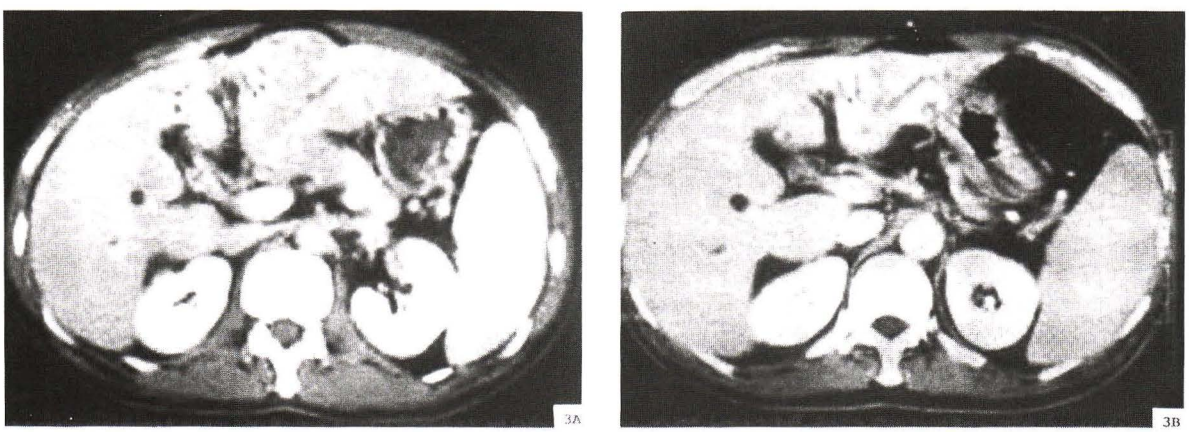
The patients tolerated the treatment procedure very well with no severe acute or late complication. No acute hepatitis and no change in liver function were demonstrated. There were 3 cases who suffered from a moderate degree pain at the end of the treatment which subsided after steroid therapy.



A. Before treatment

B. Two months after treatment

Fig. 2. A. The CT scan shows multiple nodules in both lobes of the liver with one large tumor of 10 cm in the left lobe. B. Two months after 3D-CRT, the CT scan shows marked shrinkage of the tumor in the left lobe and also in the right lobe.

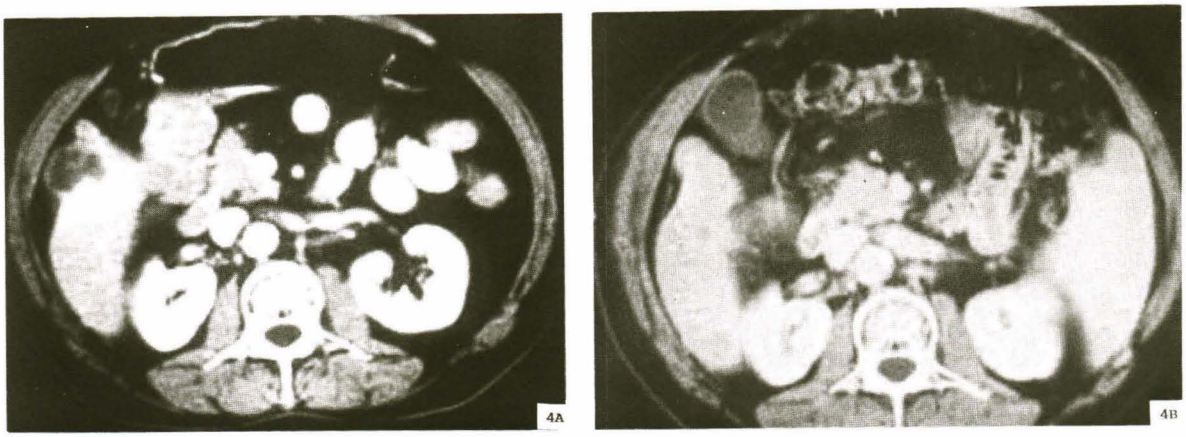


A. Before treatment

B. After treatment

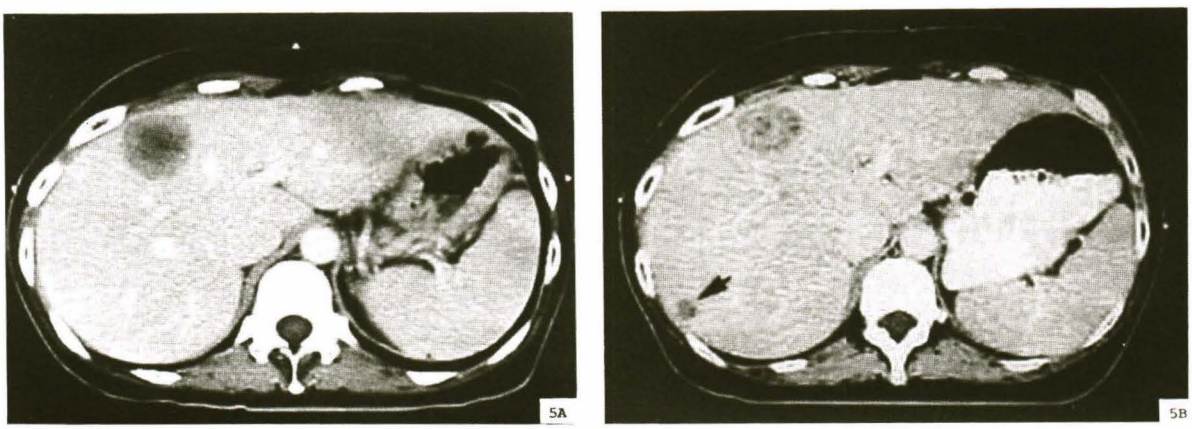
Fig. 3. A. Large hepatoma in the left lobe with compression on the stomach, caused the patient to vomit after meals. B. After 3D-CRT, the mass shows good response and compression on the stomach has been relieved.

Follow-up time was 4-20 months. The response of the treatment was determined by CT scan of the upper abdomen at 2-3 months after treatment. All treated lesions showed response with 14 partial response and 3 of complete remission. (Fig. 2-7) Pain symptoms were relieved in all cases. Alpha-fetoprotein (AFP) level had declined in all cases but in the case of relapse, rise of the AFP level cor-



A. Before treatment B. Six months after treatment

Fig. 4. The small lesion in the lower part of the right lobe (A) had disappeared at 6 months' follow-up after 3D-CRT (B).



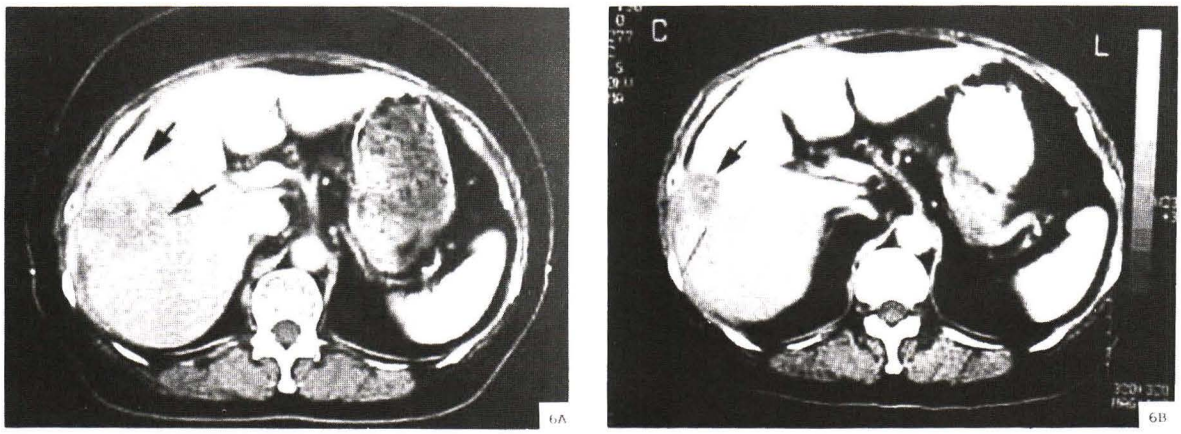
A. Before treatment B. Three months after treatment

Fig. 5. A. The CT scan shows a small hepatoma in the right lobe of the liver. B. The follow-up CT scan demonstrates regeneration in the nodule that decreased in size 3 months after treatment. Unfortunately, there is one new nodule in the lower portion of the right lobe.

responding to progression of the lesion was seen. Unfortunately, 5 cases died within one year with progression of disease (range 3 -11 months). All of those five patients had serum AFP–level over 500. Four cases were alive at 4, 12, 18 and 20 months after the treatment.

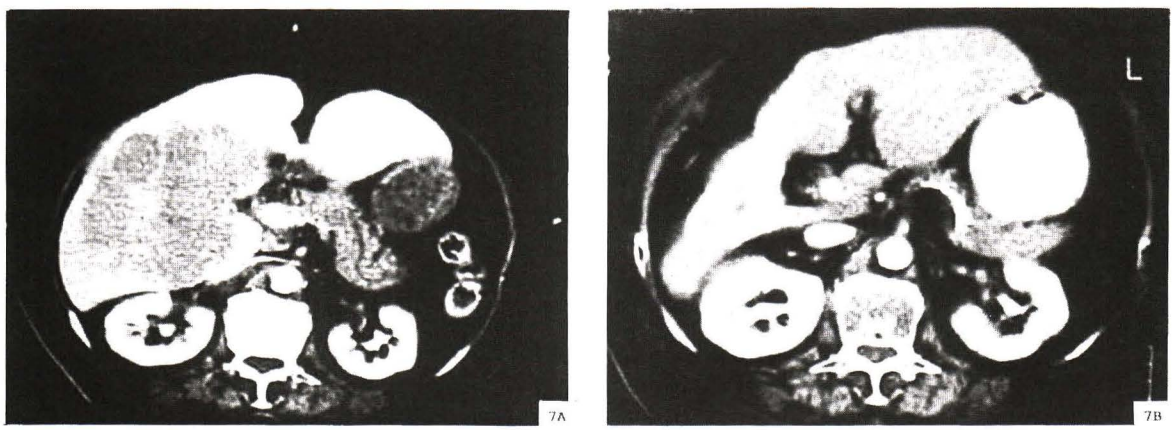
DISCUSSION

The main concern of radiation therapy is that the tumor receives enough dose to achieve a reasonable probability of local control while the normal tissue dose is low enough to keep an acceptable complication level. The target-specific treatment



A. Before treatment B. Two months after treatment

Fig. 6. A. The CT scan shows a hepatic mass of 5 cm in diameter in the right lobe. B. The mass decreased in size 3 months after completion of the treatment.



A. Before treatment B. Eighteen months after treatment

Fig. 7. A. The CT scan of a 75 year old female who presented with a large tumor nearly occupying the right lobe B. After one and a half years, the lesion disappeared, right lobe atrophy and hypertrophy of the left lobe is demonstrated.

technique is particularly desirable when a radiosensitive organ is located close to the tumor site or the tumor is located inside the vital organ. Three dimensional computerized planning system provides a mechanism to increase the tumor dose to the CT-defined target in order to enhance local tumor control and increase overall survival[9-13]. Many systems have been developed to control or determine the accuracy of positioning[14,15]. One of the most difficult problems in the treatment procedures for

this precise method is the movement of the target organ in the thorax and abdomen. Even if the body can be positioned and immobilized, the visceral organs, such as the liver, still move up and down with breathing. The conventional technique for measuring the motion of an organ is to locate landmarks in the organ and on the bony anatomy and to compare the distance between these landmarks on subsequent CT scanning. Some invasive techniques using seeds implantation were reported with unacceptable morbidity[16,17]. The extended radiation field was also used to cover this distance but lead to a decrease in the value of the conformal radiation technique. The deep breath-hold technique was then developed to solve this problem and showed a good result without any acute complications. Because the impact of radiation dose on the probability of tumor control is well established in other tumor sites and the development of 3D-CRT treatment planning has permitted us to give a high dose to the precise target, far greater doses of radiation to a liver tumor than previously used can be given[8,18]. This study warranted that high dose local radiation therapy for a hepatic tumor allowed patients with an unresectable hepatoma to receive a safety dose of 50-70 Gy which was high enough to relieve the pain symptom in all patients. With the use of active breathing control during treatments, the authors were able to decrease the amount of normal liver tissue that was forced to be irradiated on account of organ motion due to ventilation. This will lessen the risk of radiation-induced liver abnormality.

In other aspects, this precise technique can be used as radiosurgery in the organ with motion. That means, a very high dose can be given in one fraction to the tumor for curative intent. This technique might be used as an alternative treatment to surgery, especially in cases that are contraindicated for surgery.

SUMMARY

Three dimensional conformal radiation therapy and periodical irradiation with the corresponding deep inspiration breath-hold technique is a simple and feasible irradiation technique for a movable target such as a liver lesion, to decrease the toxicity of the treatment and therefore, facilitate further dose escalation. This technique should be considered as

1. Palliative treatment for relief of pain in advanced hepatoma.
2. Treatment for metastatic lesions to the liver.
3. An alternative treatment to surgery for hepatoma with a curative aim.
4. An option for treatment of a new lesion or local recurrence in a previously irradiated liver.
5. A booster technique for delivering a high dose to a well defined volume while sparing normal tissue surrounding the liver.

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การรักษามะเร็งตับชนิดเฮปาโตเซลลูลาร์ คาร์ซิโนมา โดยรังสีรักษาสามมิติและเทคนิคการฉายรังสีเป็นคาบโดยการกลั้นหายใจเป็นระยะ ๆ

พิทยภูมิ ภัทรนุธาพร, พ.บ., เยาวลักษณ์ ชาญศิลป์, พ.บ.*, นันทกานต์ เอี่ยมวนานนท์ชัย, พ.บ.*, จุมพฏ คัคนาพร, วท.ม.*, กัลยา อ่อนน้อมดี, วท.บ.**, นิรมล มั่งคั่ง, วท.บ.**, รัชนี สันติศิริ, วท.บ.***

ผู้ป่วยมะเร็งตับชนิดเฮปาโตเซลลูลาร์ คาร์ซิโนมา จำนวน 9 ราย ได้รับการรักษาโดยรังสีรักษาสามมิติ ซึ่งเทคนิคนี้ทำให้สามารถจำกัดขอบเขตการฉายรังสีให้อยู่เฉพาะตำแหน่งที่ต้องการ ทำให้สามารถหลีกเลี่ยงการฉายรังสีไปยังเนื้อตับปกติและเนื้อเยื่อปกติอื่น ๆ โดยรอบได้และยังใช้เทคนิคการฉายรังสีเป็นคาบสั้น ๆ ในระหว่างการกลั้นหายใจเป็นช่วง ๆ ของผู้ป่วย เพื่อลดการเคลื่อนตำแหน่งของอวัยวะในช่องท้องอันเนื่องมาจากการหายใจ ปริมาณรังสีที่ใช้เป็นปริมาณรังสีเทียบเท่าการฉายรังสี 50–70 Gy ครั้งละ 2 Gy สัปดาห์ละ 5 วัน โดยฉายเพียง 1–10 ครั้ง ผลการรักษาพบว่าผู้ป่วยสามารถรับการรักษาได้โดยไม่มีอาการผิดปกติหรือภาวะแทรกซ้อนใด ๆ และสามารถควบคุมรอยโรค โดยขนาดก้อนลดลง หรือบรรเทาอาการปวดแน่นท้องได้เป็นเวลา 3–20 เดือน การรักษาโดยวิธีนี้ เป็นการรักษาที่ปลอดภัยและมีประสิทธิภาพ สามารถใช้รักษามะเร็งปฐมภูมิของตับได้โดยไม่มีภาวะแทรกซ้อนต่อเนื้อตับปกติ เพื่อบรรเทาอาการในรอยโรคขนาดใหญ่ หรือรอยโรคที่มีจำนวนมาก แต่อย่างไรก็ตาม ยังคงต้องการการติดตามผลการรักษาในระยะยาวเพื่อเฝ้าระวังภาวะแทรกซ้อนที่อาจเกิดขึ้นต่อไป

คำสำคัญ : มะเร็งตับ, รังสีรักษาสามมิติ, การฉายรังสีโดยการกลั้นหายใจ

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