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Subtraction Technique in the Angiographic Assessment of Extent of Hepatocellular Carcinoma

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肝細胞癌進展範囲の血管造影診断における サブトラクション法の意義

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肝細胞癌の進展度を正確に決定するために血管造影の毛細管相のサブトラクション像を検討した。

サブトラクションは西独シーメンス製サブトラスクープ(Subtraskop)を用いた。Subtraskopは2台の閉鎖回路式テレビジョンを用いたテレビ方式のサブトラクション装置である。テレビジョンの走査線数は865本(50Hz)である。画像の記録はボラロイドカメラを使用した。

サブトラクションを行う前に60例の肝細胞癌(手術又は剖検により確認)の血管造影像を検討し、腫瘍の局在と進展範囲を記録した。その後サブトラクション法を施行して、サブトラクションを行うことによりどの程度進展範囲が増加するかを調べた。

サブトラクション法により新しく発見出来た腫瘍は右葉で7例(11.7%)、左葉にあって脊椎と重なる部位の腫瘍が12例(20.0%)、左葉にあって脊椎と重ならない部位の腫瘍3例(5.0%)であり、サブトラクション法の効果がなかった腫瘍は右葉にのみあるか、又は右葉の腫瘍濃染が明瞭であったもの15例(25%)、左葉にあるが腫瘍濃染が明瞭なもの10例(16.7%)、腫瘍が広範囲であるか、又は腫瘍血管が豊富なもの13例(21.7%)であった。

サブトラクションの有効であった症例は合計22例(36.7%)であり、サブトラクション法は血管造影による肝細胞癌の進展範囲決定には必須の補助診断法と考える。

本論文の要旨は昭和55年5月11日第39回日本医学放射線学会総会において発表した。

Introduction

Angiography plays an important and definitive role in the diagnosis of hepatocellular carcinoma (HCC), since about 15% of HCC are negative for α -fetoprotein (AFP) in our series. Angiographic diagnosis of HCC is

made on the basis of hypervascularity, tumor vessels, tumor stain, arterioportal shunt (A-P shunt), arteriovenous shunt, and their combination. Tumor stain alone cannot be considered immediately as a direct angiographic sign of HCC, although it is sometimes the only clue to the diagnosis of HCC.

Tumor stain is observed in 96.5% of cases of HCC in our series of 57 cases (1). This result prompted us to undertake the investigation whether subtraction technique improves in the detection and ascertaining the extent of the tumor or not.

We found remarkable improvement in determining the extent of the tumor by subtraction technique, and therefore the results will be reported in this communication.

Material and Method

Sixty cases of HCC were collected during the period of June, 1975 through May, 1979. These cases were studied by angiography in the department of diagnostic radiology and the pathologic diagnosis was made by either surgery or autopsy.

Subtraction technique had been used in questionable cases, but had been omitted in obvious cases in the diagnosis of malignant nature in the liver.

Angiograms in these 60 cases of HCC were reviewed before subtraction technique and the extent of the tumor was recorded in each case. In most cases this prospective diagnosis of the extent of tumor was concordant with angiographic reports.

We have then reviewed all serial angiograms, especially in the capillary phase, in 60 cases of HCC by subtraction technique and defined the extent of tumors.

The results of assessment of the extent of tumor by subtraction technique were compared with those by prospective diagnosis of extent of tumor by the naked eye.

Subtraction technique was carried out by using Siemens Subtraskop (Fig. 1a), with 865 scanning lines on the monitor at 50 Hz.

Permanent record of the subtraction image was made by photography of TV monitor using a polaroid camera.

Results

In 22 cases (36.7%) of HCC the detection rate of the tumor stain and daughter nodules was improved.

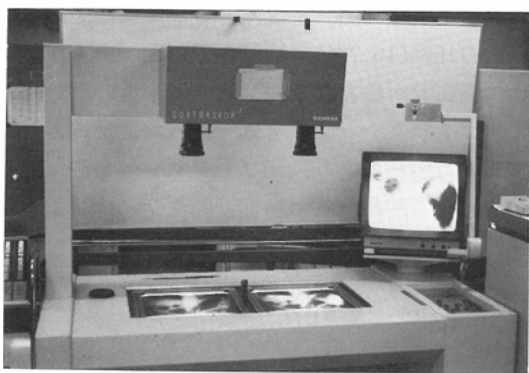


Fig. 1a Apparatus for television subtraction, Subtraskop, Siemens, West Germany. There are 865 scanning lines at 50 Hz for the television system. There is also a motor-driven zoom lens device.

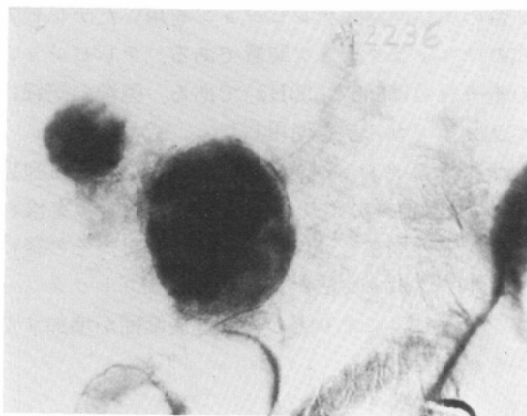


Fig. 1b Two nodules of HCC. Zoom-up image of the TV monitor in Fig. 1a. This image will exclude metastatic lesion in the left lobe superimposed on the spine.

Table 1 Contribution of subtraction technique in angiographic assessment of extent of hepatoma (60 cases)

	Subtraction technique	
	Contributory	Noncontributory
1. Tumors in right lobe detected only or much better by subtraction	7 cases (11.7%)	
2. Tumors in left lobe and superimposed on the spine, detected only by subtraction.	12 cases (20.0%)	
3. Tumors in left lobe that are not superimposed on the spine, but detected by subtraction.	3 cases (5.0%)	
4. Tumors in right lobe only or with distinct tumor stain.		15 cases (25%)
5. Tumors in left lobe only and with distinct tumor stain.		10 cases (16.7%)
6. Extensive tumors in both lobes or with marked hypervascularity.		13 cases (21.7%)
Total	22 cases (36.7%)	38 cases (63.4%)

We analyzed the reasons for improvement in the ascertaining the extent of the tumor and also for non-contributory factors of subtraction technique.

In 7 cases of HCC in the right lobe of the liver, subtraction technique was the only way to detect the tumor or to much improve the degree of tumor stain.

In 12 cases of HCC in the left lobe of the liver the tumors superimposed on the spine were detected only by subtraction technique.

These tumors seem to be undetected before subtraction due to vagueness of tumor stain superimposed on the dense spine.

In 3 cases of HCC in the left lobe of the liver of which tumors were not superimposed on the spine, the tumor stain could be detected only by subtraction technique.

In the rest of the cases the subtraction technique did not add more information regarding the extent of the tumor. Those cases are tumors limited in the right lobe with distinct tumor stain on the angiograms, tumors limited in the left lobe with distinct tumor stain, and extensive tumors in both lobes or with marked hypervascularity. Such results will be shown in Table 1.

Some of illustrative cases will be shown.

Case 1. Multinodular HCC in a 56-year-old woman,

The capillary phase of the celiac arteriogram shows multinodular type HCC with a large conglomerate of tumors in the right lobe of the liver with daughter nodules in the lateral aspect of the right lobe and also in the left lobe. However, no tumor stain is appreciated over the spine (Fig. 2a).

Multiple small daughter nodules superimposed on the spine are clearly demonstrated by subtraction technique. Metastatic nodules in the lateral aspect of the right lobe superimposed on the rib are also clearly shown (Fig. 2b).

Case 2. Solitary HCC in a 50-year-old woman.

Selective celiac arteriogram shows an apparent solitary nodule in the right lobe of the liver. The nodule had a dense tumor stain in the capillary phase. Additional tumor stains are difficult to detect (Fig. 3a).

Subtraction image clearly demonstrates additional metastatic nodules in the left lobe of the liver. A few nodules among the metastatic tumors are superimposed on the spine.

Case 3. Massive well differentiated HCC with intraperitoneal hemorrhage in a 65-year-old man.

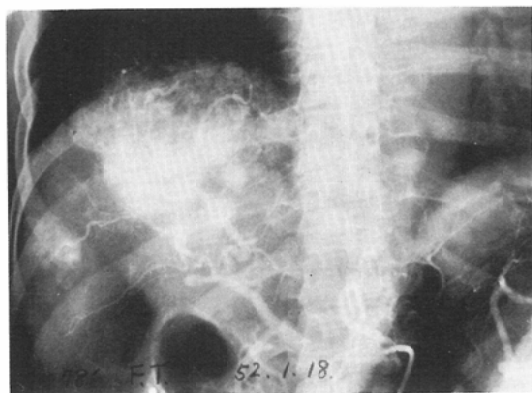


Fig. 2a Multinodular type of HCC.

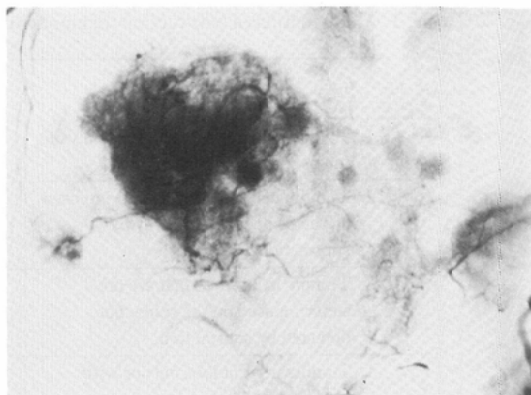


Fig. 2b Multiple small daughter nodules superimposed on the spine are clearly seen on the subtraction image, but they are not discernible in Fig. 2a.

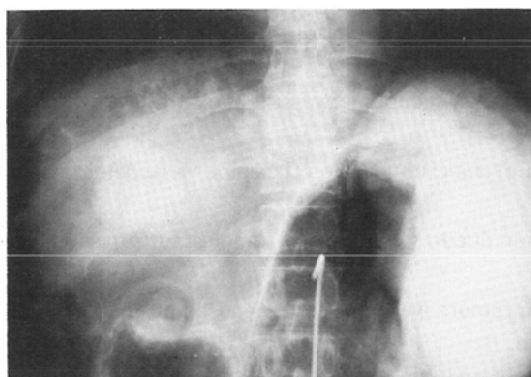


Fig. 3a Apparent solitary massive hepatoma in the right lobe of the liver.

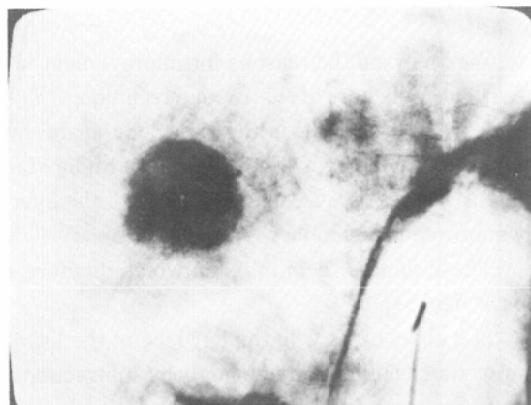


Fig. 3b Subtraction image of Fig. 3a shows distinctly additional metastatic nodules in the left lobe of the liver.

There is a large hypervascular tumor with A-P shunt (arrowhead) and central radiolucent zone occupying almost the entire right lobe. The margin is somewhat indistinct, and daughter nodules are not discernible (Fig. 4a).

Subtraction image shows a tiny daughter nodule (white arrows) medial to the large tumor. The daughter nodule is superimposed on the upper and right corner of a lower thoracic vertebra (Fig. 4b). Figure 4c is its zoom-up image. Microdensitometry of the daughter nodule on the original angiogram was carried out by Sakura PDM-5 microdensitometer. It revealed that the difference in density of the daughter nodule and its surrounding area was only about 0.15.

Case 4. Multinodular type HCC in a 77-year-old man.

There are multiple hypervascular nodules in the right lobe of the liver. There are also a few nodules in the medial segment of the left lobe (Fig. 5a).

Subtraction image clearly demonstrates not only multiple nodules but also a few small tumor stains in the left lobe, most of which are superimposed on the left margin of the thoracic spine. Thus subtraction

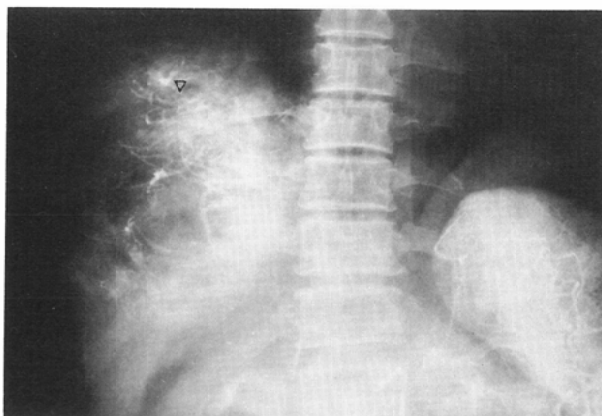


Fig. 4a A large hypervascular tumor with arterio-portal shunt (arrowhead) and central radiolucent zone in the right lobe of the liver.

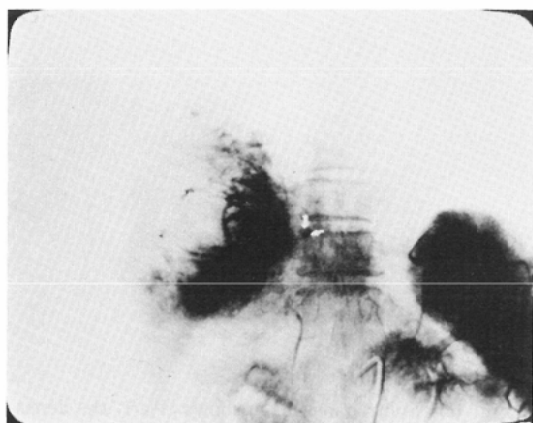


Fig. 4b A tiny daughter nodule (white arrows) medial to the large tumor. It is superimposed on the upper and right corner of a lower thoracic vertebra.

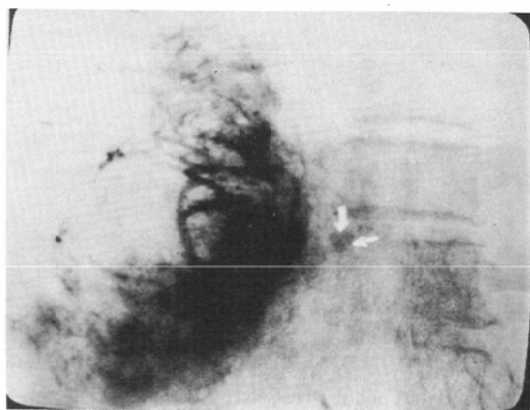


Fig. 4c Close-up view of Fig. 4b by zoom lens device.

technique clarifies metastatic nodules (Fig. 5b).

Case 5. HCC in the left lobe of the liver in a 70-year-old man. The tumor was successfully resected.

The capillary phase of the selective celiac arteriogram shows a round tumor stain in the left lobe of the liver partially superimposed on the spine (Fig. 6a).

Subtraction image shows clearly the dense tumor stain. (Fig. 6b).

Discussion

Subtraction technique was devised by Ziedses des Plantes²⁾ in 1935, and has been widely applied to various angiographic diagnosis, especially in neuroradiologic diagnosis.

Closed circuit television was applied to subtraction technique by Holman³⁾, and Shinozaki et al.⁴⁾⁵⁾, and usefull clinical application was reported by Takekawa and Holman⁶⁾.

Subtraskop made by Siemens, West Germany, has 865 scanning lines on a television monitor at 50 Hz

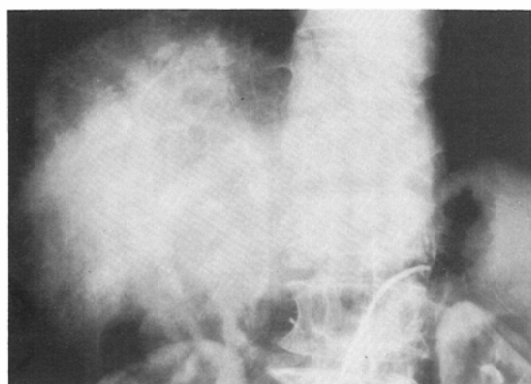


Fig. 5a Multinodular type HCC. A few nodules are also seen in the medial segment of the left lobe of the liver besides multiple nodules in the right lobe.



Fig. 5b Subtraction image clearly demonstrates a few small nodules in the lateral segment of the left lobe also.

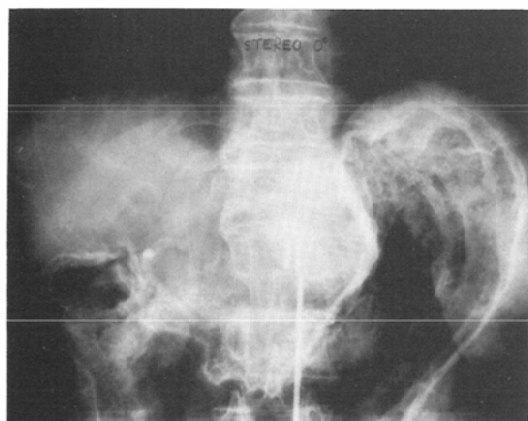


Fig. 6a A nodular HCC in the left lobe of the liver.

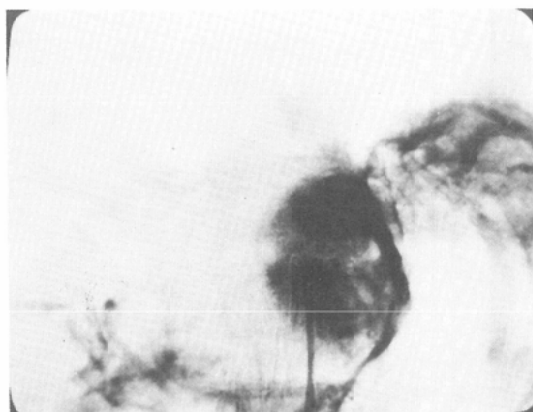


Fig. 6b Subtraction image shows clearly the dense tumor stain in the left lobe.

and has a fine detail.

It has also a zooming device to better observe the details of image by magnification.

Television subtraction method had the advantage of improving the image contrast as Wise and Ganson⁷⁾ have pointed out. Contrast enhancement by television technique is an important merit in detecting tumor stain on angiograms. This quality of improving the contrast on the film seems to be an important cause for improving the detection rate of HCC and defining metastatic nodules around the main tumor.

Angiographic assessment of the extent of HCC is very important in determining the operability since HCC is notorious for disseminating metastases in the liver via portal system.

Apparent operable case could be turned out to be an unresectable in the operating room, if widely disseminated minute metastatic tumor nodules were not found preoperatively.

We had a few such cases in which subtraction technique was omitted.

This communication is made to stress the value of subtraction technique in the detection of faint tumor stain on angiograms of HCC.

Exclusion of metastasis superimposed on the spine is easily made with considerable certainty (Fig. 1b).

We found remarkably improved detection rate of 36.7% in contrast to the previous prospective studies of

angiograms of HCC without subtraction technique. The best application of subtraction technique is to those tumors superimposed on the spine.

Some improvement in detecting and confirming the presence of tumors not superimposed on the spine was also obtained.

Subtraction technique is therefore strongly recommended in assessing the extent of HCC, especially if surgery is contemplated.

Infusion hepatic angiography (IHA)^{8,9)} has improved the quality of tumor stain and the detection rate of smaller foci of hepatic tumor by enhancing the tumor stain in the primary or secondary hepatic tumors.

In our series of angiography IHA was not yet carried out and comparison of subtraction method with IHA cannot be made. Those authors have not mentioned about subtraction technique and have not compared IHA with subtraction method. However, these two methods are important in detecting all foci of HCC and comparative study of these two methods would be desirable.

Another new and recently developed technique of angiographic imaging is digital subtraction angiography (digital venous angiography, digital fluoroscopic angiography)^{10,11,12)}. This technique has mainly applied to the diseases of the aorta, larger and moderate arteries including the renal and carotid arteries and heart. It may also be applied to hepatic angiography, but its value is to be evaluated in future.

Conclusion

Subtraction technique has improved the rate of detection of tumor and metastasis of HCC by about 37.5% in overall rate. It also makes possible to exclude metastasis with certainty.

Television subtraction is very sensitive to detect even a faint tumor stain since it has a capability to improve the contrast of the images.

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