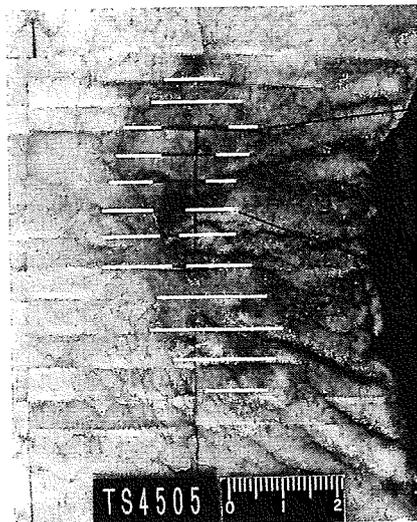


図5 切除標本肉眼像 幽門側胃切除



隆起部はmuc主体

M~SM

— MP~SS

0-IIc, T2 (SS),  
Adenocarcinoma (tub2+por, muc)  
Ly3, v0, N1

図6

認められる。図4は精検時の上部内視鏡像である。胃体下部小弯を中心に前後壁にわたり易出血性の不整粘膜が広がっており、一部に厚い白苔が附着している。全体的に厚みをもった陥凹性病変であ

り、いわゆるIIc類似進行癌と診断された。図5は切除標本肉眼像である。手術は幽門側胃切除がなされた。図6は病変範囲と深達度をマッピングしたものだが、癌は一部でSSに達しており、脈

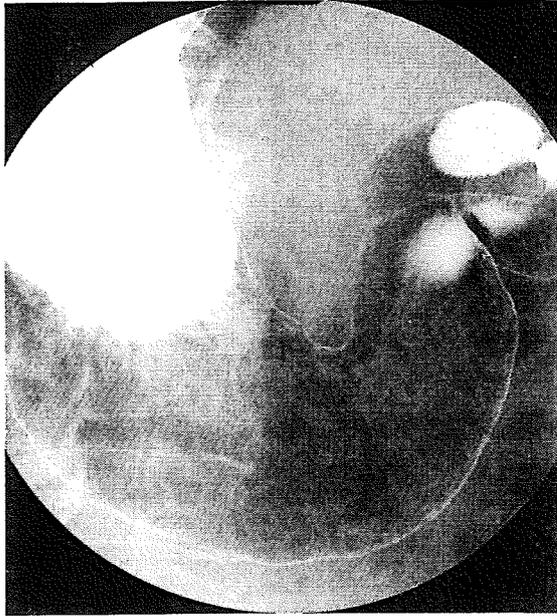


図7 発見前年度 腹臥位前壁二重造影像

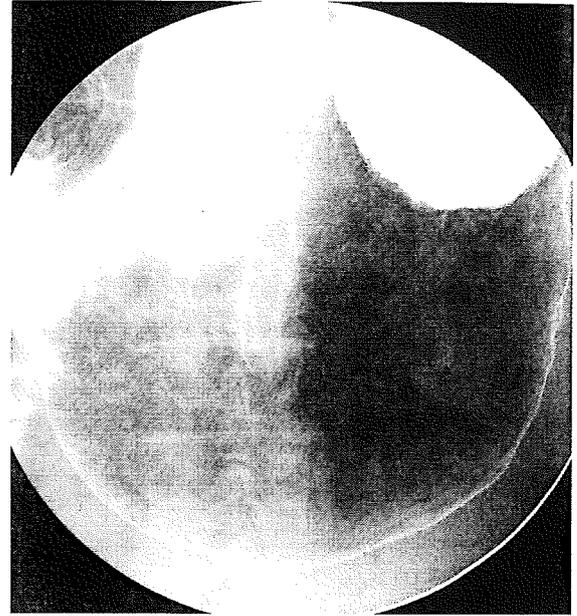


図8 発見前年度 背臥位二重造影正面像

管浸潤・リンパ節転移を認める進行癌であった。

### 考案

本症例は逐年検診にて進行癌で発見された症例である。手術根治度はAであり、救命可能な状態での癌発見という集検の目的はクリアされているのではないかと考えられる。しかし、集検の現場でもより早期での発見が望まれてきており、内視鏡治療ができる段階での拾い上げも模索されている<sup>2)</sup>。図7は発見前年度の間接撮影法・腹臥位前壁二重造影像である。胃体下部小弯に軽度の壁変形を認める。わずかに粘膜面の変化を伴っているようでもある。図8は発見前年度の背臥位二重造影正面像であるが、同部位は直線化のみの変化である。図7・8いずれも明らかな粘膜面の変化は認められず一枚のみでの拾い上げは困難である。しかし合わせて前年度の時点で拾い上げるべきであったと考えられる。なお前年度の背臥位二重造影第二斜位像は十二指腸の流出と重なってしまっていた。

辺縁の病変を二重造影像でチェックする場合、辺縁の不整や変形と言った所見のみでの拾い上げ

は擬陽性が多くなってしまうため、粘膜面の異常を伴うか否かも考慮するべきである。しかし、本症例のように辺縁所見が複数で示現されている場合（恒常性がある場合）には、粘膜面の異常が明らかでなくても拾い上げる必要があると考えられる。そのポイントを念頭において特に椎体や十二指腸と重なる部分などを注意深く読影していくことが必要であろう。最後に図9・10は平成14年・15年・16年（発見年）と病変部を拡大して並べたものである。平成14年度は腹臥位前壁二重造影像で病変部に一致して壁の硬化が疑われるが、背臥位二重造影正面像では明らかではなく、拾い上げは困難であったと思われる。ただしこのようなわずかな変化が約2年で進行癌に進行しており、逐年検診の重要性が強く実感されるとともに、読影の際には常に慎重でかつ注意深い読み込みが求められる。

発見癌について可能であれば過去にさかのぼって比較検討を行うことで、読影の質を向上させていくことが可能と考えられる。

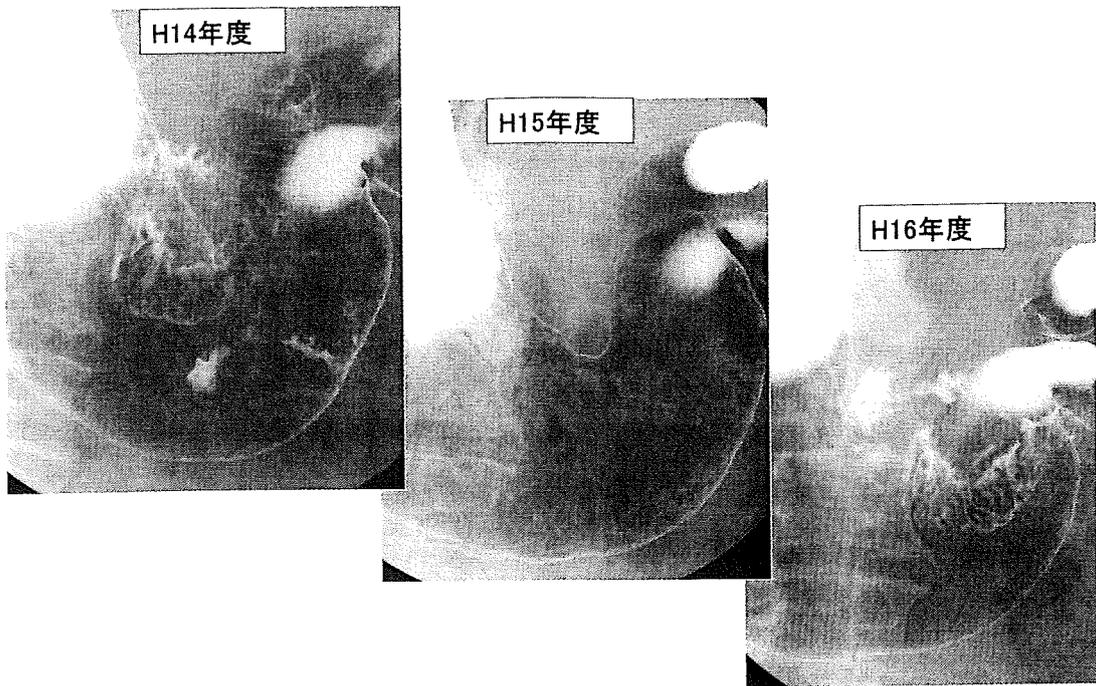


図9

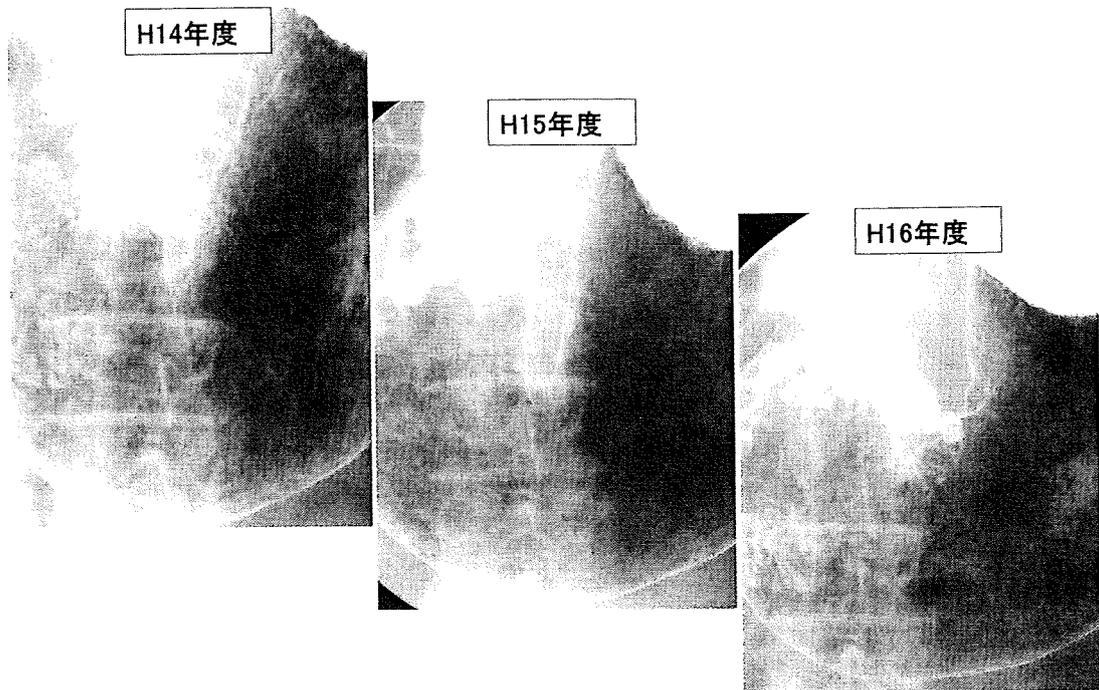


図10

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## 大腸がん検診で発見された前立腺癌の直腸浸潤例

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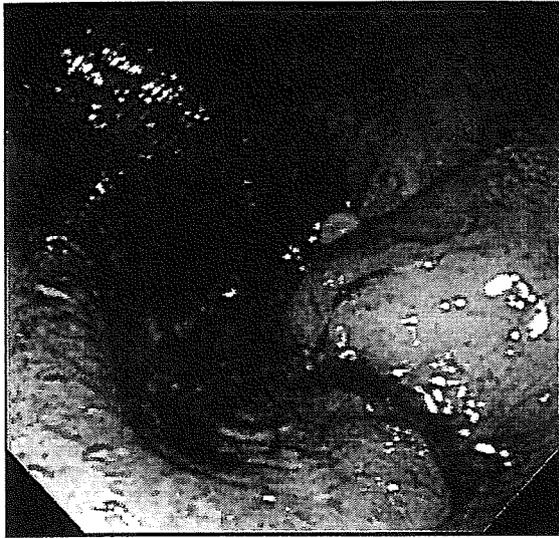


図1 内視鏡検査

### 症例

75歳男性。家族歴として妹が胃癌，既往歴には特記事項はない。1998年から2002年まで大腸がん検診を受診したが，便潜血検査は陰性だった。2003年9月頃から，血便を認めるようになった。同年9月19日に大腸がん検診を受診し，便潜血検査陽性のため同年11月に大腸内視鏡検査（図1）及び注腸X線検査（図2）を受けた。肛門から入ってすぐの前壁に2型様の病変を認め，中央の陥凹部分から生検を施行した。HE染色像（図3左）における病理医の診断は，低分化腺癌であるが，小型で均一な細胞・明るい豊かな細胞質・大型胞巣等から前立腺癌等の転移性大腸癌や内分泌系の腫瘍も否定できないというものであった。PSA及びクロモグラニンAの免疫組織染色を行ったところ，クロモグラニンA染色は陰性だったが，PSA

染色は陽性（図3右）となり，前立腺癌の直腸浸潤が強く疑われた。その後，気仙沼市立病院に紹介。前立腺針生検・CT・MRI（図4。横断像で腫瘍は前立腺の中心やや左側に存在し，矢状断像で直腸への浸潤を疑わせる。）等を施行し，前立腺癌の直腸浸潤と診断した。

### 考察

前立腺癌の直腸浸潤を正確に診断することは必ずしも容易ではないが，その理由として，頻度の少なさ，大腸精検時に前立腺癌の存在が必ずしも明らかではないこと，大腸原発の疾患に類似した形態を示すこと等が考えられる。

まず頻度に関してであるが，2000～2006年度に当施設の大腸がん住民検診で発見された原発性大腸癌は1,045例で，これに対して同時期に発見さ

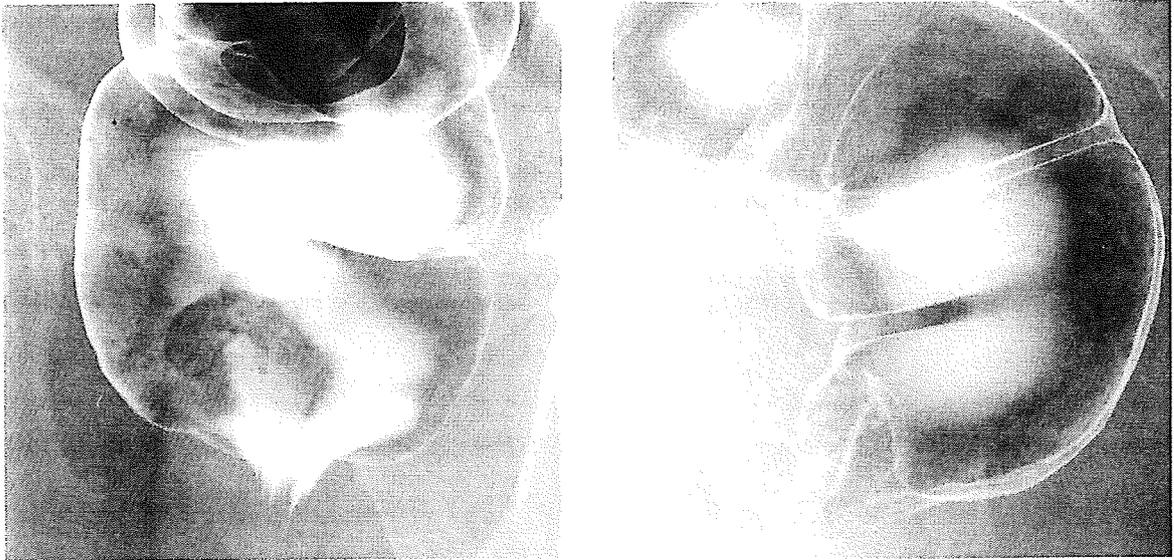
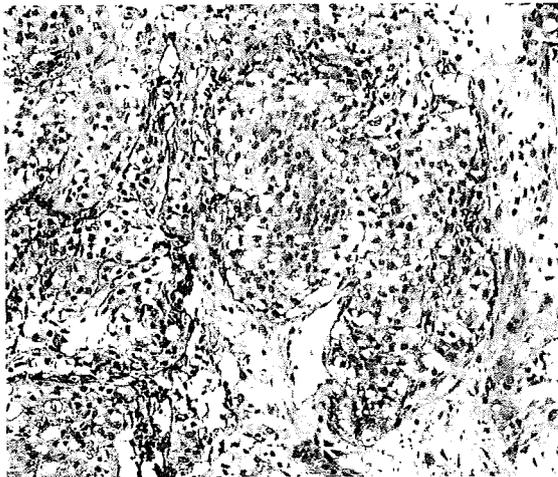


図2 注腸X線検査

HE染色



PSA免疫組織染色

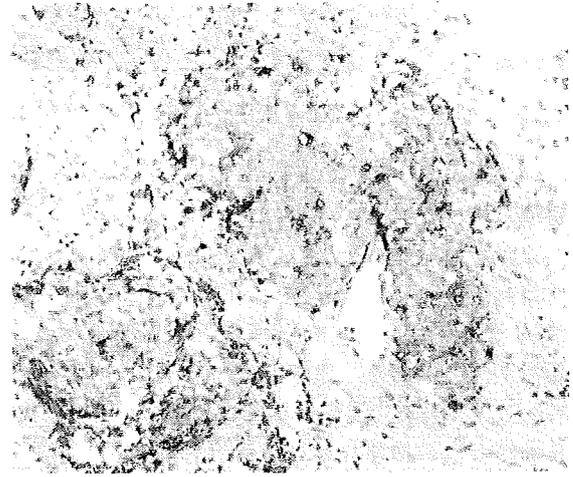


図3 生検組織

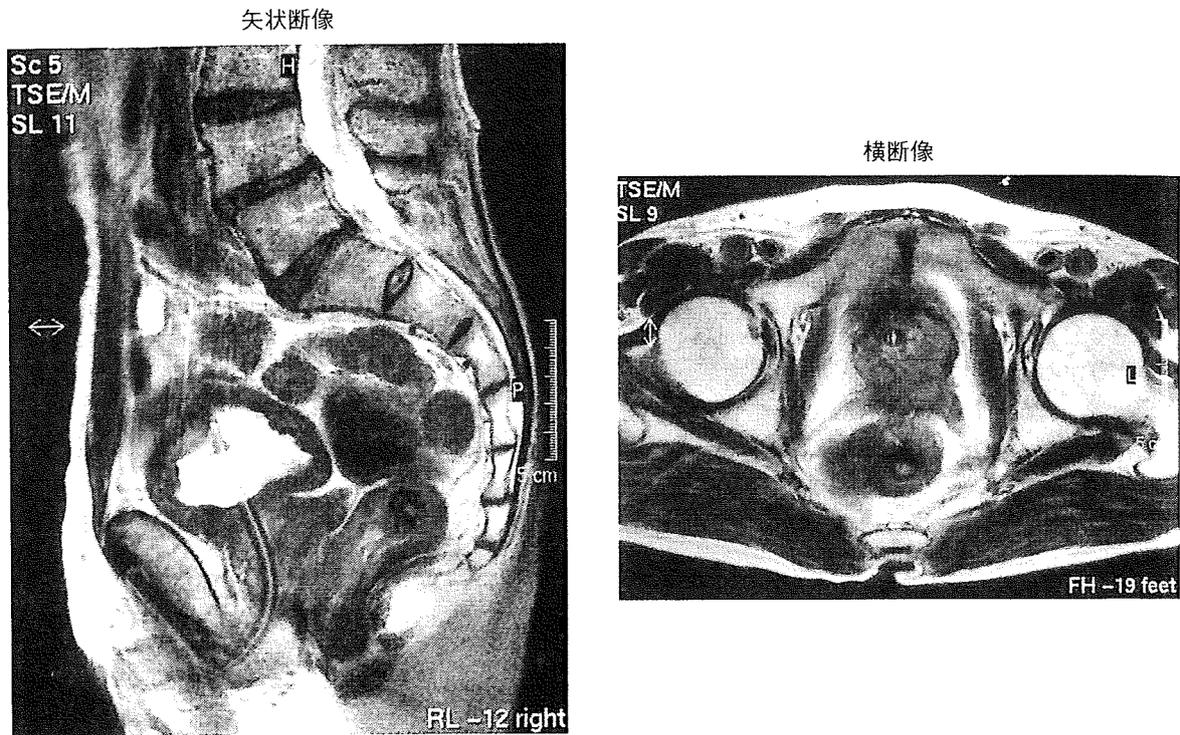


図4 MRI (T2強調像)

れた転移性大腸癌は9例と非常に少ない。更に、既報によれば、転移性大腸癌の原発部位として、胃・卵巣・子宮が多く、前立腺は少ない<sup>1)</sup>。このように大腸側から見た頻度の少なさが、前立腺癌の直腸浸潤に対する意識が希薄になり、診断を難しくさせる理由の一つである。一方で、前立腺癌の側から見ると、欧米の報告で4%<sup>2)</sup>、わが国の報告では3~6%に直腸浸潤・転移を認めたとされており<sup>3)</sup>、少ないながらも極めて稀というほどのものではない。むしろ、欧米のように前立腺癌の多い地域では、相応の発生数が見込まれる。わが国でも近年前立腺癌は増加しており、直腸浸潤例もまた増加することが考えられ、注意が必要である。

2つめの理由として、事前に前立腺癌の診断を得ているのは半数以下という報告<sup>2)</sup>があるように、大腸検査時に前立腺癌の存在が明らかでないことが多い事が挙げられる。

診断を困難にさせる3つめの理由は、大腸原発

の疾患に類似した形態を示すことであり、浸潤の機序や形態を十分理解する事が重要と思われる。前立腺癌の浸潤形態は、anterior rectal mass (I型)、annular rectal stricture (II型)、ulcerating anterior rectal mass (III型)に分けられるが、さらにseparate metastasis to rectosigmoid (IV型)を設定する報告もある。それぞれの頻度は、I型32%、II型45%、III型20%、IV型3%と報告されている<sup>2)</sup>。

浸潤形態が上記I~III型を呈する機序は、前立腺と直腸の間に存在するDenonvillier筋膜との関係で説明されている。Denonvillier筋膜は薄い前葉と強固な後葉から構成され、前立腺癌の直腸浸潤に対し抑制的に働く。この筋膜と腫瘍の関係、病変の範囲、病変粘膜の性状等は表1のように報告されており<sup>4)</sup>、いずれも大腸原発の癌や粘膜下腫瘍等に類似した形態を示す。今回の症例はIII型に該当するが、血便で気付かれ直腸癌に類似するという記載<sup>1)</sup>の通りであった。こうした臨床的特

	I 型 Anterior rectal mass	II 型 Annular rectal stricture	III 型 Ulcerating anterior rectal mass
Denonvillier 筋膜の状態	後葉は保たれている。	後葉により方向が それ、直腸周囲に 発育する。	前葉・後葉ともに 突き抜ける。
浸潤範囲	Rs～肛門管。	通常は前立腺の高 さだが、浸潤方向 で多少変動。	Rs～肛門管。
直腸粘膜	浮腫状だが、基本 的に保たれている。	浮腫状。	癌が浸潤し、潰瘍 形成。
その他	粘膜下腫瘍に類似。	4 型大腸癌に類似。 全周性ではない場 合もある。	血便で気づかれ、 2 型大腸癌に類似。 Anterior rectal mass の浸潤したタイプ。

表 1 形態別にみた前立腺癌直腸浸潤例の特徴

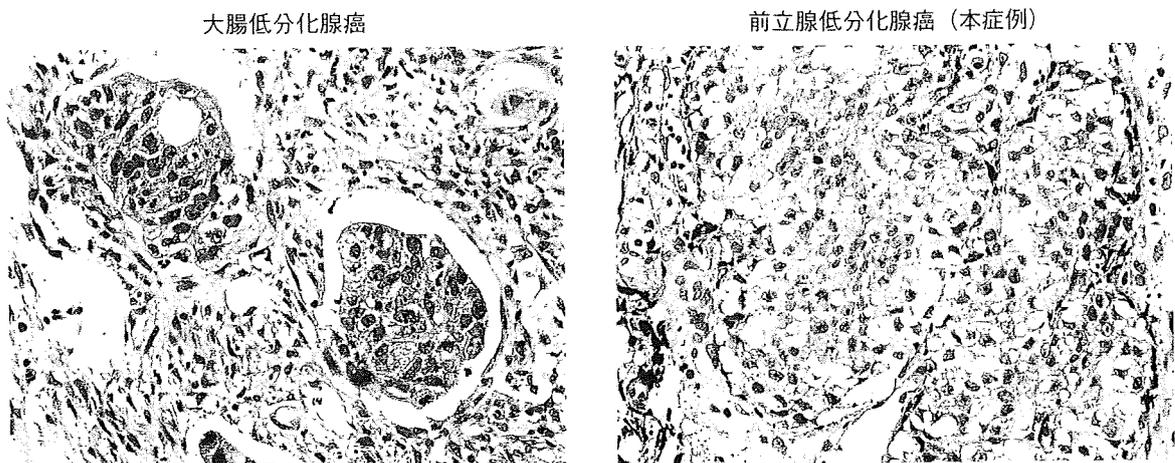


図 5 大腸と前立腺の低分化腺癌の比較

左右の倍率は等しい。大腸癌より前立腺癌の方が、細胞は小型均一で、細胞質は明るく豊かで核は小さく、大型の胞巣を形成している。

徴に加え、病理学的特徴、すなわち、HE染色では原発性大腸癌より細胞質が豊かで明るく大型の胞巣を形成すること（図5）、さらにPSA免疫染色の有効性が高いことなどを理解することで、正しい診断に至りやすくなると思われる。実際、本

症例は速やかに診断できたが、それは当施設において以前に同様の症例を経験し（表2, 図6・7）、臨床的特徴や病理学的特徴を把握していたためである。

年・性) 79歳・男性

主 訴) 便潜血検査陽性

既往歴) 特記事項なし

家族歴) 特記事項なし

現病歴) 98年, 99年に大腸がん検診を受診したが, 便潜血検査は陰性だった。

2000年6月頃から, 排便時にいつもティッシュに血が付くようになった。2000年7月大腸がん検診を受診し, 便潜血検査陽性のため同年9月に全大腸内視鏡検査を受けた。肛門から入ってすぐに2型様の病変を認めた。

表2 以前経験した同様の症例2

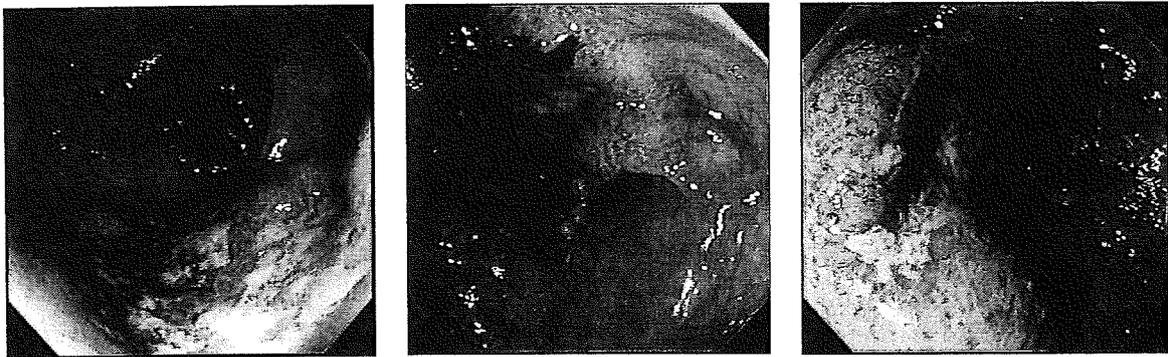


図6 症例2の大腸内視鏡所見

肛門から入ってすぐの前壁に2型様の病変を認め, 原発性直腸癌と考えた。内視鏡を反転した写真を見ると, 腫瘍の立ち上がりは健常粘膜に覆われているが, この時は深部浸潤傾向が強い性質の病変と考えていた。

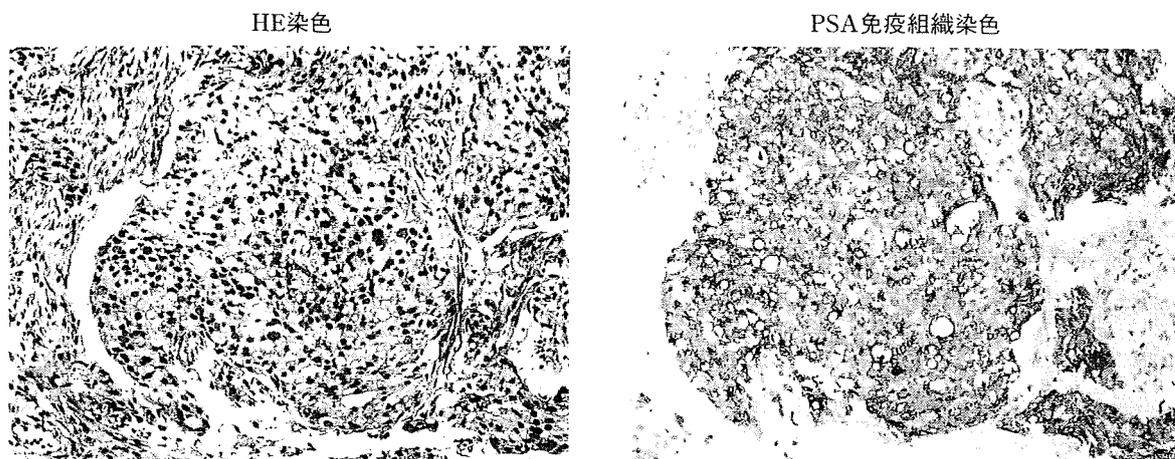


図7 生検組織の再検討結果

近医紹介後、手術が施行され、最終的には前立腺癌の直腸浸潤と診断された。図は最終診断後に生検組織を再検討したものである。

HE染色では通常の原因性大腸癌より細胞質が豊かで明るく、PSA免疫組織染色では強陽性を示した。

#### 結語

前立腺癌の直腸浸潤は大腸原発の癌や粘膜下腫瘍等に類似した形態を示すが、正確な診断のためにはその発生機序や所見を良く理解することが重要である。

#### 謝辞

ご指導ご協力を頂きました日本病理研究所の増田高行先生、気仙沼市立病院の諸先生方に深く御礼申し上げます。

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**The diagnostic validity of high-density barium sulfate in gastric cancer screening  
–Follow-up of screenees by record linkage with the Osaka Cancer Registry–**

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1 The diagnostic validity of high-density barium sulfate in gastric cancer screening

2 –Follow-up of screenees by record linkage with the Osaka Cancer Registry–

3

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24 Figures: 1

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27

28 **ABSTRACT**

29 **Background:** High-density barium sulfate was recommended by the Japan Society of  
30 Gastroenterological Cancer Screening (JSGCS) in 2004. The aim of this study is to evaluate the  
31 diagnostic validity of gastric cancer screening with high-density barium sulfate.

32 **Methods:** The study subjects were 171,833 Osaka residents who underwent gastric cancer screening  
33 tests at the Osaka Cancer Prevention and Detection Center during the period from January 1, 2000 to  
34 December 31, 2001. Screening was conducted using either high-density barium sulfate (n = 48,336)  
35 or moderate-density barium sulfate (n = 123,497). The subjects were followed up and the medical  
36 records were linked to the Osaka Cancer Registry through December 31, 2002. The results of  
37 follow-up over 1 year were defined as the gold standard; test performance values were calculated.

38 **Results:** Sensitivity and specificity of the screening test with moderate-density barium sulfate were  
39 92.3 and 91.0%, respectively, while sensitivity and specificity of the high-density barium test were  
40 91.8 and 91.4%, respectively. The results of area under receiver-operating characteristic (ROC) curve

41 (AUC) analysis revealed no significant difference between the two screening tests.

42 **Conclusion:** Both screening tests with high-density and moderate-density barium sulfate showed  
43 similar validity in terms of sensitivity, specificity, and ROC curves.

44

45 **Key words:** gastric cancer screening · barium sulfate · sensitivity · specificity · area under ROC curve

46 (AUC) analysis

47

48

## 49 INTRODUCTION

50

51 The gastric cancer mortality rate remains high in Japan, having the second highest cancer  
52 mortality rate among men after lung cancer, and the second highest mortality rate among women  
53 after colorectal cancer in 2007.<sup>1</sup> However, the rate has been decreasing in recent years, with gastric  
54 cancer screening cited as one reason for the decrease.<sup>2, 3</sup> The research group responsible for a  
55 previous report entitled “Assessment of Effectiveness of New Screening Techniques for Cancer”  
56 concluded that there exists reasonable evidence of a reduction in gastric cancer mortality following  
57 mass screening for gastric cancer using fluoroscopy.<sup>4</sup>

58 High-density barium sulfate was recently developed and is used in many medical facilities; the  
59 guidelines of the Japanese Society of Gastroenterological Cancer Screening (JSGCS) in 2005  
60 recommended its use for gastric cancer screening.<sup>5</sup> There is no clear definition of high-density

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61 barium sulfate, but the suggestion of 180 w/v% and 150 ml, as provided by Doi et al.,<sup>6</sup> is generally  
62 accepted. The temperature of the barium, and the pH and volume of gastric juice have little influence  
63 on the viscosity of high-density barium sulfate,<sup>7,8</sup> and it has better acid resistance and fluidity than  
64 does moderate-density barium sulfate.<sup>9</sup> As a result, high-density barium sulfate has the advantage of  
65 superior depiction of the gastric mucosa,<sup>10-13</sup> and it is easy for screenees to drink.<sup>9,13-15</sup> It has the  
66 disadvantages of rapid outflow from the stomach<sup>16,17</sup> and increased incidence of mis-swallowing.<sup>14</sup>  
67 <sup>18</sup> Hamashima et al.<sup>19</sup> conducted a systematic review of existing data and reported that the superiority  
68 of high-density barium sulfate could not be confirmed because there has been no improvement in the  
69 rate of gastric cancer detection or early gastric cancer detection.<sup>10,20-22</sup> They recommended further  
70 appropriate research to clarify the diagnostic validity of the new method.

71 The aim of the present study is to analyze whether the new method using high-density barium  
72 sulfate has better diagnostic validity for gastric cancer than does the conventional method using  
73 moderate-density barium sulfate, in terms of sensitivity, specificity, and area under receiver-operating  
74 characteristic (ROC) curves (AUC).<sup>23</sup> Linkage of the records with the Osaka Cancer Registry  
75 enabled follow-up of screenees.<sup>24</sup> The diagnostic validity of the gastric cancer screening test has been  
76 reported by Murakami et al., using this system.<sup>25</sup> Although evaluations of the diagnostic validity of  
77 the gastric cancer screening test have also been performed in other prefectures in Japan,<sup>26, 27</sup>  
78 evaluation of the diagnostic validity of screening with high-density barium sulfate has yet to be  
79 conducted using AUC analysis. The present study is the first in Japan to clarify the diagnostic  
80 validity of the gastric cancer screening test with high-density barium sulfate.

81

82

83 **METHODS**

84

85 **Subjects**

86       The protocol for this study was approved by the Ethical Committee of the Osaka Cancer  
87 Prevention and Detection Center. The study subjects were 171,833 Osaka residents who underwent  
88 gastric cancer screening tests at the Center between January 1, 2000 and December 31, 2002. The  
89 subjects were screened by either the new method using high-density barium sulfate ( $n = 48,336$ ),  
90 conducted at the Center or at mobile units, or by the conventional method using moderate-density  
91 barium sulfate ( $n = 123,497$ ) at mobile units.

92

93 **Materials and Radiographic Methods**

94       The moderate-density barium sulfate suspensions used in this study were Barytgen sol 145  
95 w/v% sol, 200 ml (FUSHIMI Pharmaceutical Co., Ltd., Marukame, Japan) and Baritop sol 150  
96 w/v% sol, 200 ml (Kaigen Co., Ltd., Osaka, Japan). The high-density barium sulfate suspensions  
97 were Baribright P 185 w/v% powder, 160 ml (Kaigen Co., Ltd.) and Barytgen HD 200 w/v%  
98 powder, 145 ml (FUSHIMI Pharmaceutical Co., Ltd.). Gastric cancer screening was performed  
99 using 10 mobile screening units and 2 fluoroscopic devices at the Osaka Cancer Prevention and  
100 Detection Center; U-MA5N (Hitachi Medical Co., Ltd. Tokyo, Japan) and ZS-40 (Shimadzu Co.,

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101 Ltd Kyoto, Japan). Radiographs were obtained using image-intensifier fluorography with 100 mm  
102 roll film. Kodak PFH-T FILM (Eastman Kodak Co., Ltd, Rochester, N Y.) and Fuji M1-FA  
103 (FUJIFILM Corporation, Kanagawa, Japan).

104 The new method (high-density barium sulfate) was recommended by the Japan Society of  
105 Gastroenterological Cancer Screening (JSGCS)<sup>5)</sup> The images obtained using this method were as  
106 follows: (1) double-contrast view in the supine position, (2) double-contrast view (lower) in the  
107 prone position, (3) double-contrast view (upper) in the prone position, (4) right anterior oblique  
108 position, (5) left anterior oblique position (lower), (6) left anterior oblique position, (7) semi-erect in  
109 the left anterior oblique position, and (8) semi-erect in the right anterior oblique position. The images  
110 obtained using the conventional method (moderate-density barium sulfate<sup>28)</sup> were as follows. (1)  
111 anterior mucosal view in the prone position, (2) barium-filled view in the prone position, (3)  
112 double-contrast view in the supine position, (4) left anterior oblique position, (5) right anterior  
113 oblique position, (6) semi-erect left anterior oblique position, and (7) barium-filled view in the erect  
114 position. The above-mentioned seven or eight shots were used as the basis of the imaging  
115 examination; extra shots were obtained by the radiological technologists when necessary.

116

#### 117 **Screening Test and Follow-Up Methods**

118 The gastric cancer screening was examined by 19 radiological technologists and 20  
119 radiologists at the Osaka Cancer Prevention and Detection Center Images from the new method  
120 (high-density barium sulfate) and the conventional method (moderate-density barium sulfate) were

121 examined by the same radiological technologists and by the same radiologists. All radiologists and  
122 radiological technologists examined images produced from both radiographic methods. A  
123 double-check system with two radiologists was used for film reading. The radiographic findings  
124 were divided into five groups as follows: A: definitely cancer, B: probably cancer, C: possibly cancer,  
125 D: suspicious of a benign lesion, E: workup tests for confirmation.<sup>29</sup>

126 To detect false-negative cases, we conducted follow-up by linking the gastric cancer screening  
127 records from the Screening Center with the files of the Osaka Cancer Registry through December 31,  
128 2003. References for individual identification were name, sex, birth date, and address. Cases of  
129 cancer detected within 1 year of the screening day were considered as cancer present at the time of  
130 screening, and the sensitivity and specificity were calculated.<sup>30</sup> Sensitivity and specificity were also  
131 calculated by sex group (male, female), age group ( $\geq 60$ ,  $< 60$ ) and all subjects (both sexes and age  
132 groups). Sensitivity and specificity of high-density barium sulfate screening was compared with that  
133 of moderate-density barium sulfate screening. We evaluated the diagnostic validity of gastric cancer  
134 screening for high-density and moderate-density barium sulfate.

135

### 136 **Statistical analyses**

137 The Cochran–Mantel–Haenszel test was used to analyze the age and sex distribution of the  
138 subjects. The chi-square test was used to analyze the results of the screening, sensitivity and  
139 specificity. AUCs were compared using the algorithm developed by DeLong et al.<sup>23</sup> The diagnostic  
140 validity of high-density barium sulfate screening compared with moderate-density barium sulfate

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141 screening was analyzed using AUC values. Difference with  $P < 0.05$  was considered significant.  
142 These statistical analyses were performed using SPSS 15.0 J for Windows (SPSS Japan Inc., Tokyo,  
143 Japan). AUC for the two barium sulfate screening were analyzed using Stata 9.2 for Windows  
144 (StataCorp LP, College Station, TX).

145

146

## 147 RESULTS

148

149 Table 1 shows the sex and age distributions of the screenees in the high- and  
150 moderate-density barium sulfate tests. The male/female ratio was greater than 1 in the high-density  
151 test, and less than 1 in the moderate-density test. The mode for age in the high-density test was  
152 50–59 years among both males and females; in the moderate-density test, the mode for age was  
153 50–59 years among females and 60–69 years among males. There was significant difference in the  
154 sex and age distributions of screenees between the high- and moderate-density barium sulfate tests ( $P$   
155  $< 0.05$ ).

156 Comparison of the results of screening between the two barium sulfates is shown in Table 2.  
157 The proportion of screenees for whom workup examination was recommended (screening positives)  
158 was lower for high-density (8.7%) than for moderate-density barium sulfate (9.2%) ( $P = 0.001$ ). The  
159 proportion of screenees who underwent workup examinations was 86.8% for the moderate-density  
160 barium sulfate test and 85.6% for the high-density test ( $P = 0.044$ ). The gastric cancer detection rate

161 was 0.17% for moderate-density and 0.13% for high-density barium sulfate, and the proportion of  
162 early gastric cancer detected was 67.6% for moderate-density and 62.9% for high-density barium  
163 sulfate.

164 Table 3 shows a comparison of the results of follow-up with linkage of records with the Osaka  
165 Cancer Registry, and Table 4 shows a comparison of the results of follow-up by sex (male, female)  
166 and age ( $\geq 60$ ,  $< 60$ ). All false-negative cases (6 cases in the high-density test and 19 cases in the  
167 moderate-density test) were detected by follow-up using the record linkage to the cancer registry.  
168 Some true-positive cases (5 cases in the high-density test and 20 cases in the moderate-density test)  
169 were not known by routine collection of data regarding examination work-ups, but were discovered  
170 for the first time via follow-up with the record linkage to the cancer registry.

171 Table 5 shows the test performance values of screening with the two barium sulfates by all  
172 subjects. The predictive value of positive tests was 2.00% for moderate-density barium sulfate and  
173 1.59% for high-density barium sulfate. No significant difference was found for sensitivity (92.28%  
174 for moderate-density barium sulfate and 91.78% for high-density barium sulfate). Significant  
175 difference was found for specificity (91.43% for high-density barium sulfate and 90.98% for  
176 moderate-density barium sulfate;  $P = 0.003$ ). Table 6 compares sensitivity and specificity between  
177 the two barium sulfates by sex (male, female) and age group ( $\geq 60$ ,  $< 60$ ). No significant differences  
178 were observed in terms of sensitivity in all categories. Although specificity was a significant  
179 difference between the two barium groups by sex group (male, female) ( $P = 0.000$ ,  $P = 0.031$ ),  
180 significant differences were not found by age group ( $\geq 60$ ,  $< 60$ ).