Above: View of Interactive Atlas, showing selected anatomical structures (left) and cross section of human anatomy (right) corresponding to the above EUS image.

**VHJOE** is an interactive online journal utilizing a powerful tool: the **Visible Human Interactive Atlas**. This web-based application, developed by the Center for Human Simulation, provides unparalleled views of human anatomy. By loading models of selected organs, and manipulating an image plane, unique images of human anatomy are created **realtime** and loaded into your browser window.
# Table of Contents

**Editor’s Column**

*Visible Human Journal of Endosonography*  
Volume No. 2  
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Year 2003

## Articles

- Occult Gastrointestinal Bleeding of the Lower and Upper Intestine  
  Diagnosed by Capsule Endoscopy and Treated by Argon Plasma Coagulation  
  Steven J. Squillace, M.D. & John C. Deutsch, M.D.  
  Page: 2

- Sclerosing Mesenteritis: A Report of Two Cases with Dramatic Response  
  to Immunosuppressive Agents  
  William R. Brown, M.D., William W. McIntyre, M.D. & Peter R. McNally, D.O.  
  Page: 3

## Reviews

- Endoscopic Ultrasound For Rectal Cancer  
  Gregory G. Ginsberg, M.D. & Nuzhat Ahmad, M.D.  
  Page: 7

- EUS in the Literature  
  Manoop S. Bhutani, M.D.  
  Page: 11

## Technical Updates

- Tips for Using the Visible Human Interactive Atlas  
  David Rubinstein, M.D. & Karl Reinig, Ph.D.  
  Page: 12

## Featured Movie

- Visible Human: Upper Thorax  
  John C. Deutsch, M.D.  
  Page: 8

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Editor’s Column || John C. Deutsch MD

Evolution of VHJOE Continues

With this sixth issue of VHJOE, we are announcing more changes to the journal. We are continuing to evolve as we seek to improve VHJOE and make better use of the expanding capabilities of the internet.

First, icons placed next to article titles inform the reader of features included in that article. The icons indicate if the article contains images from the Visible Human Interactive Atlas, video clips, and/or audio clips.

We are also trying to make the features more intuitive. For example, in the past, any image in the journal could be enlarged by clicking on it. This may not have been evident. Starting with this issue, we are making the targets and features easier to find and utilize.

In addition, we now accept and publish audio clips. An example of an audio clip is included with this editorial [Audio Clip 1 available on-line only at www.vhjoe.org] and another one can be heard with the featured movie column. We encourage prospective authors to submit audio and video clips, along with other appropriate images.

Finally, the editorial board has also decided to expand the field of content for the journal. VHJOE wants to publish image driven articles, and we felt that there are many times an very visual article of interest exists in which EUS played no part. Furthermore, there are expert reviews, which are very noteworthy and visually instructive beyond the field of EUS. We have therefore changed the name of the journal from the Visible Human Journal of Endosonography to the Visible Human Journal of Endoscopy. Our expert reviews this year will include the following topics: capsule endoscopy, CT-colography, endoscopic ampullectomy, and mother-daughter biliary endoscopy. We hope this broadening focus is beneficial to our readers.

This month our expert review is by Dr. Ginsburg and Dr. Ahmad on the utility of EUS in rectal cancer. This is a valuable resource both for physicians who perform EUS and also for gastroenterologists at large, to emphasize the valuable role EUS plays in the management of patients with this condition. Figure 1 shows an image from the Visible Human Female data set that correlates to some of the EUS images in this review. The image has a small “3” over the vagina and a “2” at the base of the bladder.
Occult Gastrointestinal Bleeding of the Lower and Upper Intestine Diagnosed by Capsule Endoscopy and Treated by Argon Plasma Coagulation

Introduction: Occult gastrointestinal bleeding can be a difficult challenge in clinical medicine. This case demonstrates the utility of new technologies in the diagnosis and therapy of occult bleeding separate localities in the gastrointestinal tract.

Methods for EUS Capture: SVHS tape of endoscopy was digitally captured using Dazzle Movie Star software. Givens Capsule film clips were captured using the Givens software. Film clips were combined using Adobe Premiere 6.0.

Case: A 64-year-old man was evaluated for occult gastrointestinal bleeding. The patient has had chronic transfusion-requiring blood loss anemia for the previous four years. Evaluations at three different medical centers including two upper endoscopies, a barium small bowel follow through, two colonoscopies, and capsule have all been negative to date.

The patient received transfusions every two to four weeks to keep his hemoglobin greater than or equal to 10.5 g/dl. He presented with a hemoglobin was 8.8g/dl and black “like coal” stools which were new for him.

His past history includes mitral valve replacement and chronic coumadin therapy, and underlying coronary artery disease. His physical exam revealed stable vital signs, a mechanical click consistent with an artificial heart valve, and dark stool.

An upper endoscopy was performed which was unremarkable. This was followed by a capsule endoscopy. The capsule endoscopy revealed active bleeding in the colon (Figure 1). A colonoscopy was performed, which demonstrated several large angiodysplastic lesions in the right colon, which were cauterized using argon plasma coagulation (Video Clip 1).

A model from the Visible Human Interactive Atlas (Figure 2) shows the location of the bleeding site seen at capsule endoscopy.

The patient seemed to stabilize, but after a few weeks, was noted to again have a falling hemoglobin. A repeat colonoscopy showed other large angiodysplastic lesions in the right colon which were again treated with argon plasma coagulation. Over the next few weeks, the dark stools persisted, and transfusions were again required. The patient was admitted in anticipation of a right hemicolectomy.

On admission, the patient had stable vital signs, dark stools, a hemoglobin of 7 g/dl, and a prolonged INR at 4.8. Plasma was given, and his coagulopathy corrected with vitamin K. The patient was then placed on heparin. Since he was a relatively high surgical risk, the patient was given a cleansing colonic preparation and a preoperative capsule endoscopy was performed (eight weeks after the previous capsule endoscopy) to insure there were no bleeding sites outside of the anticipated surgical field.

Active hemorrhage was seen in the duodenum by capsule endoscopy (Figure 3). An upper endoscopy revealed an ongoing bleeding site which was treated with argon plasma coagulation (Video Clip 2). The Visible Human Interactive Atlas model of the duodenum shows the location of the bleeding site seen at endoscopy (Figure 4).

Since the latest treatment, the patient’s hemoglobin has remained stable, and he is now being followed as an outpatient.

Discussion: Angiodysplasia is a well-described cause of bleeding from both the upper and lower gastrointestinal tract (1-5). If not actively bleeding, the offending site can be difficult to identify, as these vascular anomalies are often small and may be multiple.

Our case exemplifies the difficulties in diagnosing this condition, in that his evaluations at several centers were unremarkable, despite upper and lower endoscopies and a capsule endoscopy. Even though this patient had an initial negative capsule endoscopy at an outside center, this case shows that the advent of capsule endoscopy has significantly improved the diagnostic abilities of physicians involved in caring for subjects with occult bleeding.

The treatment of angiodysplasia has generally been through thermal methods. Recently, argon plasma coagulation has become a preferred thermal method to treat bleeding in many centers (6,7), and appears to be quite effective as shown in our case.

A unique feature of our patient was the documentation of hemorrhage by capsule endoscopy at two very distinct ends of the gastrointestinal tract at two separate times during the patient’s course. The second capsule endoscopy performed in our center was fortuitous in finding active bleeding in the duodenum which prevented a planned right hemicolectomy. Capsule endoscopy has been recently introduced into clinical practice, and is rapidly becoming a procedure of choice in the evaluation of occult gastrointestinal bleeding.
bleeding (8).

Based on the patient’s previous course of events, it would not be surprising if this particular patient returns with more bleeding in the future. Based on our recent experience, we would likely begin our next evaluation with capsule endoscopy in this interesting individual.

References:

Article || William R. Brown, M.D., William W. McIntyre, M.D. & Peter R. McNally, D.O.

Sclerosing Mesenteritis: A Report of Two Cases with Dramatic Response to Immunosuppressive Agents

Introduction: Inflammatory and fibrotic diseases of the mesentery are rare, and detailed reports of response to their treatment are few. We here report two patients with sclerosing mesenteritis who responded dramatically to treatment with prednisone or with prednisone plus azathioprine.

Body:
Patient 1
A 37-year old Moroccan national, who has lived in the United States for the past twelve years, complained of diarrhea, bloating, and weight loss for four months. He had been in generally good health except for complex partial seizures since 1991 (treated with valproic acid) and depression (treated with sertraline). He was unemployed but had worked in food preparation and sales. He recalled no serious illness while living in Morocco and had no other foreign travel, but had worked in food preparation and sales.

His laboratory values are given in Table 1. A computer tomogram (CT) image of the abdomen is shown in Figure 1.

An upper gastrointestinal and small bowel radiographic series demonstrated delayed transit through the ileum and sharp angulation and fixation of ileal loops, suggestive of an adhesive or fibrotic process. Upper gastrointestinal endoscopy revealed thick folds in the gastric body and diffuse gastritis. At enteroscopy, the small bowel to the mid-jejenum appeared normal. Histologically, gastric biopsies had chronic gastritis, with mixed T-cell and B-cell populations identified by immunohistochemical stains for CD20 and CD3 markers, and negative Congo red stain; Helicobacter pylori were present. The small bowel biopsies had a few areas of intestinal lymphangiectasia. Eosinophilia was not present in any of the biopsies.

Laparoscopy was attempted. An umbilical port was placed but only after the peritoneum was incised sharply because of its “thickness and toughness”. Abdominal exploration was impossible because of inflammatory adhesions (Figure 2). The characteristics of the ascitic fluid obtained at laparoscopy are given in Table 2. The serum albumin-ascitic fluid albumin gradient was 1.4, consistent with a transudative effusion.

Next, laparotomy was attempted. The peritoneum was extremely (5-mm) thick, and extensive digital dissection was required to separate it from

Figure 1: Patient 1, computerized tomogram of the abdomen. Loculated fluid (arrow) and fluid insinuated between small bowel loops is present. In other views, the fluid extended from the mid pelvis along the anterior abdominal wall to the level of the celiac axis.

Figure 2: Laparoscopic view of Patient 1. Serosanguinous intraabdominal fluid, a thick, fibrous peel over the small bowel (star); and fibrous bands between small bowel loops are evident.

Figure 4: A model of the duodenum from the Visible Human Interactive Atlas showing the approximate site of the duodenal bleeding (red dot).

Video Clip 2: A combined video clip showing the duodenal bleeding by capsule endoscopy; the active duodenal bleeding by upper endoscopy and argon plasma coagulation of the duodenal bleeding site.
Table 1: Laboratory Values
(ND indicates Test Not Done)

<table>
<thead>
<tr>
<th>Test</th>
<th>Patient 1 (normal range)</th>
<th>Patient 2 (normal range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hematocrit</td>
<td>38.9% (38.0-52.0)</td>
<td>22.5% (42-45)</td>
</tr>
<tr>
<td>Mean corpuscular volume</td>
<td>87.9 μm³ (80-100)</td>
<td>77 μm³ (80-100)</td>
</tr>
<tr>
<td>White blood cell count</td>
<td>10.6/mm³ (4.5-10)</td>
<td>12.5/mm³ (4.5-11)</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>0.3% (0-5)</td>
<td>0.1% (0-6)</td>
</tr>
<tr>
<td>Platelet count</td>
<td>304 x 10⁹/μL (150-400)</td>
<td>300 x 10⁹/μL (150-400)</td>
</tr>
<tr>
<td>Erythrocyte sedimentation rate</td>
<td>ND</td>
<td>144 mm/hr (0-13)</td>
</tr>
<tr>
<td>C-reactive protein</td>
<td>ND</td>
<td>180 mg/L (0-8)</td>
</tr>
<tr>
<td>Serum protein, total</td>
<td>6.7 g/dL (6.0-8.2)</td>
<td>6.3 g/dL (6.8-8.6)</td>
</tr>
<tr>
<td>Serum albumin</td>
<td>3.8 g/dL (3.4-5.5)</td>
<td>1.6 g/dL (3.4-5)</td>
</tr>
<tr>
<td>Serum pre-albumin</td>
<td>ND</td>
<td>9 mg/dL (18-45)</td>
</tr>
<tr>
<td>Serum alkaline phosphatase</td>
<td>76 IU/L (40-117)</td>
<td>532 IU/L (50-136)</td>
</tr>
<tr>
<td>Alanine aminotransferase</td>
<td>15 IU/L (5-40)</td>
<td>53 IU/L (20-65)</td>
</tr>
<tr>
<td>Serum bilirubin, total</td>
<td>0.4 mg/dL (0.2-1.2)</td>
<td>0.9 mg/dL (0.1-2.1)</td>
</tr>
<tr>
<td>Serum glucose</td>
<td>75 mg/dL (60-115)</td>
<td>160-204 mg/dL (70-100)</td>
</tr>
<tr>
<td>Urinary protein</td>
<td>0-2+ (negative)</td>
<td>977 mg/24 h (10-150)</td>
</tr>
<tr>
<td>Fecal α₁-Antitrypsin</td>
<td>ND</td>
<td>5.0 mg/g wet weight (&lt;2.6)</td>
</tr>
<tr>
<td>Serum immunoglobulin A</td>
<td>ND</td>
<td>1060 mg/dL (79-356)</td>
</tr>
<tr>
<td>Anti-nuclear antibody</td>
<td>Negative (negative)</td>
<td>Negative (negative)</td>
</tr>
<tr>
<td>Serum iron</td>
<td>42 μg/dL (40-160)</td>
<td>12 μg/dL (40-150)</td>
</tr>
<tr>
<td>Serum iron binding capacity</td>
<td>274 μg/dL (220-420)</td>
<td>138 μg/dL (275-4000)</td>
</tr>
<tr>
<td>Iron saturation</td>
<td>15% (16-55)</td>
<td>8.7% (16-55)</td>
</tr>
<tr>
<td>Serum lipase</td>
<td>43 U/L (16-63)</td>
<td>165 U/L (115-285)</td>
</tr>
</tbody>
</table>

Table 2: Ascitic Fluid Analyses
(ND indicates Test Not Done)

<table>
<thead>
<tr>
<th>Test</th>
<th>Patient 1</th>
<th>Patient 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance</td>
<td>Serosanguinous</td>
<td>Yellow, clear-hazy</td>
</tr>
<tr>
<td>Erythrocytes</td>
<td>49,680/μL</td>
<td>100/μL</td>
</tr>
<tr>
<td>Leukocytes</td>
<td>30/μL</td>
<td>230/μL</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>2%</td>
<td>1/μL</td>
</tr>
<tr>
<td>Glucose</td>
<td>21 mg/dL</td>
<td>118 mg/dL</td>
</tr>
<tr>
<td>Albumin</td>
<td>2.4 g/dL*</td>
<td>1.2-1.4 g/dL**</td>
</tr>
<tr>
<td>Total protein</td>
<td>4.0 g/dL</td>
<td>5.2 g/dL</td>
</tr>
<tr>
<td>Amylase</td>
<td>ND</td>
<td>18U/L</td>
</tr>
<tr>
<td>Triglyceride</td>
<td>40 mg/dL</td>
<td>ND</td>
</tr>
<tr>
<td>Lactic dehydrogenase</td>
<td>244 IU/L</td>
<td>74 IU/L</td>
</tr>
</tbody>
</table>

*Serum albumin/ascitic fluid albumin gradient 1.4
**Serum albumin/ascitic fluid albumin gradient 0.2-0.4

Note: Multiple cytopathologic examinations for malignant cells; cultures for fungi, acid-fast bacilli, aerobic bacteria and anaerobic bacteria; and stains for acid-fast bacilli were negative in both patients’ fluids. In addition, viral cultures were negative in the fluid of Patient 1, and no Mycobacterium tuberculosis complex RNA was detected by polymerase chain reaction in the fluid of Patient 2.
what appeared to be the bowel. No visible landmarks could be identified on the bowel surface, and no motility was seen. Nodular adhesions that were very difficult to separate prevented any further dissection.

Histopathologically, the peritoneal biopsies were characterized by extensive areas of hyalinized connective tissue, scattered foci of mixed inflammatory cells, and spindle cells (Figures 3A and 3B). No granulomas or foreign-body reactions were present. In immunohistochemical stains, a few of the spindle cells were positive for CD117 (c-kit proto-oncogene product) but negative for CD34 (1,2); mitoses and cellular atypia were not seen. Thus, it was concluded that the patient did not have a gastrointestinal stromal tumor (1). Stains for acid-fast bacilli and fungi were negative. By flow cytometric analysis, a polyclonal population of plasma cells was found, and the CD15 stain for Reed-Sternberg cells of Hodgkin’s lymphoma was negative (3). The histologic findings were felt most consistent with the diagnosis of sclerosing mesenteritis.

Prednisone orally at 40 mg per day was begun. Within a few days the patient’s appetite and tolerance for food had markedly improved, and his sense of well being returned. Taking his current dose of prednisone, 5 mg per day, he has no abdominal symptoms. He has not been treated for H. pylori infection. An abdominal CT scan performed four weeks after the initiation of prednisone revealed that the ascites was absent, but some signs of mesenteritis persisted (Figure 4).

**Patient 2**

A 54-year old Vietnam War veteran had a four-month history of right upper quadrant abdominal pain, early satiety, vomiting and 35-pound weight loss. He had non-insulin-dependent diabetes mellitus; coronary artery disease, with coronary artery by-pass grafts; hypertension; ankylosing spondylitis; bilateral hip prostheses for degenerative joint disease; an aneurysm is present (star). On other views, the gastric wall was very thick and the spleen enlarged, with granulomas present.

His laboratory values are given above in Table 1. A CT image of the abdomen is illustrated in Figure 5. Upper gastrointestinal endoscopy showed increased folds and decreased motility in the gastric antrum, suggestive of a malignancy. A H. pylori urease test was negative. Endoscopic ultrasound examination of the stomach confirmed thickening of the gastric wall (Figure 6). Cytologic and flow cytometric analysis of gastric wall material obtained by fine-needle aspiration revealed a mixed population of lymphocytes and granulocytes, with no malignant or monoclonal B-cells. Enteroscopy showed a normal-appearing small intestine to the mid-jejunum. The colonoscopy could not be completed because of poor preparation but was normal to the hepatic flexure.

Histologic evaluation of biopsies obtained at endoscopy revealed mild, chronic gastritis and fundic gland hyperplasia, without features suggestive of Menetrier’s disease or the presence of H. pylori; the small intestinal and rectal morphology was normal. No evidence of amyloidosis, eosinophilia, lymphoma, granulomatous disease or acid-fast bacilli was present in any of the biopsies. The serum IgA concentration was elevated, but this was considered to be a monoclonal IgA-kappa gammapathy of undetermined clinical significance on the basis of histologic, flow cytometric and immunohistologic examination of bone marrow biopsy material. Abdominal ultrasound examination demonstrated hepatosplenomegaly and normal blood flow in all hepatic vessels. Liver tissue obtained via transjugular biopsy was normal except for mild cholestasis, and the portal pressure/hepatic vein gradient was normal.

Laparoscopy was attempted, but a grossly thickened peritoneum and loculated septations surrounding yellow ascitic fluid were encountered; a pneumoperitoneum could not be achieved and the procedure was abandoned (Figure 2).

Next, laparotomy was attempted. The omentum, mesentery and bowel were encased in a thick peel. All structures were densely adherent and impossible to dissect safely. The adhesions were felt much different from those usually encountered in a postoperative patient or associated with other intra-abdominal pathology. No free planes were found, and it was impossible to see the liver or other abdominal organs.

The histologic features of the operative biopsies are illustrated in Figures 7A and 7B. Various stains for microorganisms, including acid-fast bacilli and fungi, were negative. A pancytokeratin stain revealed proliferation of spindle mesothelial cells, but no evidence of malignancy. The findings were felt consistent with the diagnosis of sclerosing mesenteritis; peer review of the sections by the Armed Forces Institute of Pathology concurred.

Postoperatively, the patient was treated with prednisone orally (initially, 60 mg per day, then tapered to 6 mg per day) and azathioprine, 50 mg per day. His appetite, sense of well being and tolerance of food improved markedly, beginning 3-4 weeks after starting the immunosuppressive treatment. After a few months he had gained weight from 110 to 170 pounds despite losing all leg edema and clinically appreciable ascites. Azathioprine has been continued at 50 mg per day. Attempts to reduce the prednisone dosage below 6 mg/day have resulted in a recurrence of abdominal symptoms. The serum albumin has risen to 2.8 mg/dL. Several months after his laparotomy his abdominal

**Figure 3A:** Peritoneal biopsy tissue from Patient 1, shown in Figure 3B.

**Figure 3B:** Higher magnification of an area of the peritoneal biopsy tissue from Patient 1, shown in Figure 3A.

**Figure 4:** Abdominal CT findings in Patient 1 four weeks after the start of prednisone therapy. The ascites has completely resolved, but loops of small bowel appear adherent to one another.

**Figure 5:** Abdominal CT image of Patient 2. Loculated ascites (arrows) and retraction of the mesentery are evident. A 5-cm abdominal aortic aneurysm is present (star). On other views, the gastric wall was very thick and the spleen enlarged, with granulomas present.
aneurysm ruptured, and because his mesenteritis prevented surgical repair, endograft placement of a stent graft was performed. A CT scan of his abdomen taken 15 months after his laparotomy showed much resolution of ascites, but changes resulting from the ruptured aortic aneurysm made other comparison with earlier CT scans difficult.

Discussion:

Chronic inflammatory and fibrotic conditions of the mesentery are rare (4,5). They have a spectrum of overlapping clinical and histologic features, and have been designated by many different names (4,5). So-called retractile mesenteritis, also known as sclerosing mesenteritis, represents the fibrotic end of the spectrum, whereas the inflammatory end has been called mesenteric panniculitis, mesenteric lipodystrophy and other names (4). Histologically, our patients have predominantly a fibrotic form of mesenteritis, although inflammatory features also are present; they lack a characteristic feature of mesenteric panniculitis, i.e., multinucleated giant cells (6). A wide variety of constitutional and abdominal symptoms and signs may be associated with the various mesenteritides; our patients manifested principally inability to eat or to retain food, weight loss, abdominal pain and large-volume ascites. Gastrointestinal protein loss, a reported feature in sclerosing mesenteritis (7), was documented in Patient 2 by the presence of increased loss of fecal α1-antitrypsin.

The cause of chronic mesenteritis is unknown, as in our cases. Neither patient had known exposure to toxic agents or the use of medications that have been causally linked to retroperitoneal fibrosis, i.e., methylsregide and ergotamine (4). Abdominal trauma or previous abdominal surgery could not be implicated. Our exhaustive search for malignancies or infectious diseases was negative, and the patients’ favorable response to immunosuppressive therapy belies the possibility that such diseases were undetected. We have found no reports of sclerosing mesenteritis associated with chronic inflammatory bowel disease (which Patient 2 was reputed to have had but could not be confirmed), ankylosing spondylitis, autoimmune diseases, or the use of the medications our patients were taking. Patient 1 had gastric H. pylori infection, but Patient 2 did not, so infection with that organism cannot be implicated. Despite the many similarities in our patients’ illnesses, we can find no common etiologic link; they are markedly dissimilar in nationality, ethnicity, occupation and military experience.

The natural history and treatment of chronic, fibrotic forms of mesenteritis are not well documented. Although mesenteric panniculitis seems to have a good prognosis and may regress spontaneously (4,5), the outcome in sclerosing mesenteritis seems less favorable. We believe it unlikely that our patients’ diseases would have resolved without medical treatment since both men had been ill for months, and their disease was progressing. Their response to treatment with immunosuppressive agents was dramatic and prompt. Although similar improvement has been recorded among a few such patients treated with cyclophosphamide (8), corticosteroids alone (7), corticosteroids together with colchicine (9) or azathioprine (10,11), the reported experience with these agents still is small. Moreover, radiologic resolution or improvement of the ascites or fibrosis, as in our patients, has been documented infrequently (8,12). Thus, the outcome in our two patients is a significant addition to the literature on this subject. On the basis of recorded experience it seems reasonable that immunosuppressive agents be tried in the pharmacologic treatment of idiopathic chronic mesenteritis, although some patients have not responded to the agents and a few have responded to other categories of drugs, i.e., oral progesterone (12) and tamoxifen (13). The impressive responses of idiopathic mesenteritis to immunosuppressive agents suggest that the condition has an immunologic pathogenesis, but that possibility awaits verification.

References:

Endoscopic Ultrasound For Rectal Cancer

Introduction: Colorectal cancer is among the most common cancer affecting adult men and women. There are nearly 38,000 new rectal cancers diagnosed each year in the United States. While part of a functional continuum, rectal cancers are distinguished from colon cancers based on some very real anatomic, prognostic, and practical differences. These differences command staging and therapies unique to rectal lesions. Stage-based therapy for rectal cancer has achieved broad acceptance and is considered the standard of care. This submission reviews the role of EUS for the evaluation and management of rectal cancers.

Body: Rectal Anatomy

The rectum originates beneath the peritoneal reflection, extending 15 cm to 20 cm from the anal verge. The rectum is contained within the narrow pelvis, confined by the pubic bones anteriorly and the lumbosacral spine and coccyx posteriorly, and surrounded by structures vital to urinary and sexual function. Using trans-rectal EUS, the urinary bladder, seminal vesicles, prostate and urethra are well seen in the male (Figure 1A and 1B). The urinary bladder, uterus, and vagina are less well appreciated in women (Figure 2).

The anatomy of the anorectum is specifically designed for storage and controlled evacuation of the fecal bolus. Defecation and continence require the coordinated interaction of several muscular structures in and surrounding the anorectum. The circular muscle of the anus forms a prominent internal anal sphincter, which provides tonic closure of the anus. Specialized skeletal muscles descending from the levator ani apparatus provide a muscular sling and terminate to form the external anal sphincter. When viewed with a radial scanning echoendoscope at the level of the anal verge, the internal and external anal sphincters can be viewed as two distinct rings (Figure 3) (1). The lymphatic drainage of the rectum follows the route of its venous drainage along the inferior, middle, and superior hemorrhoidal veins to the inferior mesenteric veins and along the iliac veins and onto the portal vein.

Rectal Cancer

The prognosis for rectal cancer correlates with the pathologic stage at the time of diagnosis. So too, management is predicated on tumor stage at diagnosis and response to induction therapy. A wide variety of surgical techniques have been developed for rectal neoplasms in consideration of the anatomic constraints, preservation of function, and intent to achieve cure (2). These are associated with disparate rates of postoperative morbidity. Cancer containing superficial villous adenomas can be cured with endoscopic mucosal resection (EMR). Lesions confined to the wall may be resected by transanal excision or low anterior resection. Lesion involving, or in close proximity to, the anus may warrant abdominoperineal resection preserving anal sphincter function. Patients with locoregionally-advanced lesions (extension onto the perirectal fat and/or perirectal or pelvic adenopathy) should be considered for neoadjuvant chemoradiation. Neoadjuvant therapy has been demonstrated to reduce local recurrence and permit increased likelihood of a sphincter-sparing operation with less toxicity when compared to post-operative regimes (3). Thus, unlike more proximal colon cancer, the optimal method of management for rectal carcinomas is critically dependent on the accurate preoperative staging of the disease as shown below in Table 1 (4).

<table>
<thead>
<tr>
<th>Tumor Stage</th>
<th>Location</th>
<th>Treatment Option</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polypoid T1</td>
<td>N0</td>
<td>TAEX</td>
</tr>
<tr>
<td>Sessile T1</td>
<td>N0</td>
<td>LAR</td>
</tr>
<tr>
<td>T2, N0/ High</td>
<td></td>
<td>LAR</td>
</tr>
<tr>
<td>T2, N0/ Low</td>
<td></td>
<td>TAEX or APR</td>
</tr>
<tr>
<td>T2, N0/ Low</td>
<td></td>
<td>NAT followed by LAR</td>
</tr>
<tr>
<td>T2, N0/ High</td>
<td></td>
<td>NAT followed by APR</td>
</tr>
<tr>
<td>T2 or T4, any N/ High</td>
<td></td>
<td>NAT followed by APR</td>
</tr>
<tr>
<td>T2 or T4, any N/ Low</td>
<td></td>
<td>NAT followed by APR</td>
</tr>
</tbody>
</table>

Table 1: EUS tumor stage and lesion location determines treatment options for rectal cancers.

Note: High = ≥ 2cm from dentate line; Low = < 2cm from dentate line; EMR = endoscopic mucosal resection; TAEX = transanal excision; LAR = low anterior resection; APR = abdominoperineal resection; NAT = neoadjuvant therapy.

Equipment and Technique:

Endorectal Ultrasound (ERUS) can be performed either with blind, rigid probes or with flexible echoendoscopes. This discussion will focus on the use of flexible echoendoscopes. The Olympus GF-UM series of echoendoscope is the standard instrument for staging. This is an oblique-viewing (fiber optic or electronic video image) instrument. The tip contains a miniature ultrasound transducer that provides a 360-degree radial image perpendicular to the long axis of the scope at ultrasound frequencies of 5.0 MHz, 7.5 MHz, 12 MHz, or 20 MHz. Piezoelectric curvilinear array scopes are used.
for EUS-guided fine needle aspiration of extraluminal lymph nodes.

ERUS is an ambulatory procedure. Patients prepare the rectum with two Fleet’s enemas in advance. Intravenous sedation is optional. With the patient in the left-lateral-decubitus position, digital rectal exam (DRE) should be performed. DRE should allow assessment of sphincter tone and palpation of the lesion. If palpable, the lesion should be described in terms of location, distance from the anal verge, and fixation or mobility. Forward viewing sigmoidoscopy should be performed to image the lesion both in the forward and retroflexed scope positions (Figure 4). This allows familiarity with the anatomic configuration of the patient’s rectum and the location and distribution of the tumor.

The echoendoscope is inserted and advanced beyond the lesion, under direct vision, to the rectosigmoid junction. ERUS imaging should begin at 5.5-7.5 MHz during withdrawal of the scope. The lumen is deflated of air and the water-fill balloon adjusted for acoustic coupling. Tip deflection should be passive allowing the transducer to find the right axis to the lumen. During this phase of the exam, surrounding adenopathy is the quarry. Any lymph nodes seen should be interrogated for size, shape, and echotexture (Figure 5). The scope is withdrawn to the level of the anal verge.

Next, the tumor itself should be targeted to determine depth of penetration into or through the rectal wall. The choice of frequency is dependent on the lesion size but 7.5 and 12 MHz frequencies are most commonly employed for T-staging. The degree of tip deflection and water-balloon fill should be adjusted to avoid false-findings owing to tumor compression, tangential imaging, and air artifact. Water-filling the lumen through the accessory channel is often necessary to achieve optimal imaging (Figure 6). The echoendoscope is withdrawn over the lesion to achieve satisfactory imaging over the length of the lesion. Lastly, the scope is withdrawn to the anal verge to interrogate anal sphincters for tumor invasion. Sphincter interrogation is an active process and should incorporate voluntary squeezing and relaxation of the muscles during imaging.

ERUS Staging of Rectal Cancer
The American Joint Committee of Cancer has identified the TNM classification as the preferred staging system (5). This system is based on the determination of depth of tumor invasion (T-classification), the presence of regional lymph node metastases (N-classification), and the presence of distant metastases (M-classification). The individual classifications are combined to provide an overall stage.

EUS Tumor Stage
Endosonographically, the rectal wall is seen as five alternating hyper- and hypoechoic layers (Figure 7). The histologic correlation of the echolayers is as follows:

First layer (hyperechoic) - interface between water or water-filled balloon and the superficial mucosa.
Second layer (hyperechoic) - represents the deep mucosa and the muscularis mucosa.
Third layer (hypechoic) - represents the submucosa and its interfaces.
Fourth layer (hyperechoic) - represents the muscularis propria.
Fifth layer (hypechoic) - interface between the serosa and perirectal fat.

Rectal cancer appears as homogeneous hypechoic soft tissue. Invasion appears as disruption of the normal wall echolayer pattern. A tumor that by EUS appears to be limited to the mucosa or the submucosa (first three echo layers) is classified as a T1 lesion (Figure 8A-8E). A tumor that invades into the muscularis propria (the hypechoic fourth EUS layer) is a T2 lesion (Figure 9). A T3 lesion penetrates through the rectal wall, extending beyond the five echo layers and into the surrounding perirectal fat (Figure 10). A T4 lesion displays direct invasion into an adjacent organ such as the prostate gland, sacrum, vagina, and bladder (Figure 11).

EUS Lymph Node Staging
Endosonographically, lymph nodes appear as round or oval structures, which are hypechoic compared to the surrounding perirectal fat (Figures 5 and 11). Endosonographic criteria applied to perilesional adenopathy in other regions of the digestive tract for the determination of malignancy versus benignity may not be so well applied in rectal cancer. Data obtained primarily in patients with esophageal carcinoma so have identified four sonographic criteria predictive of malignancy: large size (>1cm), hypechoic echodensity, sharply demarcated borders, and round (rather than ovoid or flat) shape (6). These criteria may not apply so well to rectal carcinoma. An accuracy of about 50% of metastatic lymph nodes associated with rectal cancers are smaller than 5mm (7). While EUS guided fine needle aspiration (FNA) of an individual lymph node might confirm accuracy, it is only rarely called upon for this purpose in initial staging.

Accuracy of EUS in Staging Rectal Cancer
Accuracy of tumor and nodal staging is dependent on the experience and expertise of the endosonographer (8). The overall accuracy of T-staging for rectal cancer varies between 70% to 90% (9-17). When EUS is incorrect for T-staging, it is typically due to under-staging rather than over-staging. EUS tends to overstage cancers because high-resolution ultrasound can detect, but not separate inflammation adjacent to the malignancy from the tumor itself. Under-staging is attributed to undetected microscopic invasion of cancer cells beyond that observed by EUS. Accuracy is generally lowest for lesions classified as T2 by EUS, which may be overstaged as T3 lesions. Over-staging is apt to occur when imaging tumors located on a haustral fold, due to artifact induced by...
tangential imaging. Water-filling the rectal vault will improve technical results and likely enhances T-stage accuracy.

The overall accuracy of N-staging by EUS is 73% to 83% (9-16). Lower nodal staging accuracy is attributed to the observation that up to 50% of malignant nodes are less than 5 mm in diameter and EUS detection rates of these nodes may be as low as 20% (7).

Nonetheless, ERUS has been reported to be equal to or superior to computed tomography (CT) for T and N staging. Among several comparative studies, EUS has a greater accuracy than CT scan for staging of rectal cancer: 67% to 93% versus 53% to 86% for T-stage and 80%–87% versus 57% to 72% for N-stage (19–21). Magnetic resonance imaging (MRI) with endorectal surface coils has compares similarly but not better that EUS in accuracy (22-26).

While there is little published experience for EUS-FNA for rectal cancer, experience extrapolated from other malignancies has suggested that the performance of fine needle aspiration cytology can markedly increase the accuracy and specificity of EUS nodal classification. Management may be altered when nodal metastasis is identified in a patient in whom T-classification would otherwise suggest the possibility of local endoscopic or transanal resection as a curative option. This applies to the 10% of patients with T1 lesions that have positive lymph nodes.

Restaging after Neoadjuvant Therapy
Pre-operative neoadjuvant chemoradiotherapy is commonly used to down-stage rectal cancers. In addition to improving long-term survival and local recurrence, this approach allows sphincter preserving LAR in many patients who would require APR based on findings at initial presentation. Neoadjuvant therapy of rectal cancer results in tumor regression/necrosis and inflammatory and fibrotic changes in the rectal wall (Figure 12). These changes may be sonographically indistinguishable from viable tumor. As such, accuracy of T and N – staging after chemoradiation therapy is considerably compromised (27). Therefore, we do not apply TNM staging when inspecting lesions for response to preoperative chemoradiation therapy. Rather we assess evidence for tumor regression from surrounding organs, in particular the anal sphincters, vagina, and prostate. In this way EUS can direct therapy in patients who have undergone neoadjuvant therapy as a prelude to possible sphincter-sparing surgery (28).

EUS for Local Recurrence of Colorectal Carcinoma
Local recurrence of rectal cancer after presumed curative resection occurs in 10-15% of cases, usually within the first two years after surgery. It is hypothesized that early detection of recurrent local tumor prompting early re-treatment would improve survival. While this notion may be logical, it remains unproved. EUS may be useful in the detection of suspected local recurrence when no mucosal lesions are seen during surveillance sigmoidoscopy. Preliminary data obtained using blind/rigid ultrasound probes suggested that transrectal ultrasound was highly sensitive for the detection of anastomotic recurrence (29, 30). A more recent study using a radial scanning echoendoscope reported EUS as highly sensitive (>90%) in the detection of local rectal tumor recurrence (31). However, the sonographic changes of local tumor recurrence are not specific. Post-operative and post-radiation inflammatory/fibrotic changes have similar appearances (32). EUS should be used to complement sigmoidoscopy when local recurrence is suspected. In these instances, extraluminal local recurrence suspected by EUS can be confirmed by EUS-guided fine needle aspiration (Figure 13).

Summary:
EUS is the most accurate tool for local staging of rectal carcinoma. In addition to providing accurate T- and N- stage, EUS allows assessment of the internal and external anal sphincters. Accurate endosonographic staging directs the optimal method of management of rectal cancer: type of resection, and candidacy for neoadjuvant therapy. Repeat sigmoidoscopic and endosonographic imaging may be considered in selected patients following neoadjuvant therapy. EUS guided FNA can be used to detect suspected local recurrence.

References:
Figure 10: Hypoechoic T3 tumor disrupts the entire wall layer pattern with invasion into the perirectal fat. A hypoechoic band at top demarks preservation of the prostate’s integrity.

Figure 11: The T4 tumor (T) pictured endoscopically in figure 4 demonstrates direct extension into the wall of the urinary bladder (B) (1:00 position). A suspicious lymph node is also seen (LN) (5:00 position).

Figure 12A: A T3 tumor is seen at presentation (as shown here). Following neoadjuvant chemoradiotherapy, a shallow ulceration persists where once a bulky tumor existed (as shown in Figure 12B). On EUS the scarred wall at the tumor remnant site is hypoechoic and has lost the five-layer wall pattern (as shown in Figure 12C). The tumor has receded away from the prostate. A small peri-lesional lymph node is appreciated. At surgical pathology, no residual carcinoma was identified.

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**Figure 13A:** An extrinsic compression is seen at sigmoidoscopic investigation for local recurrence (as shown here). EUS showed a focal hypoechoic perirectal soft tissue mass. Transrectal EUS guided fine needle aspiration (as shown in Figure 13B) provided cytological confirmation of adenocarcinoma.

**Figure 13B:** See caption on Figure 13A.

**EUS in the Literature || Manoop S. Bhutani, M.D.**


This prospective study investigated the potential clinical and economic benefits of EUS in 485 patients suspected to have choledocholithiasis based on clinical, biochemical, and cross-sectional imaging (US or CT) data. Positive EUS findings were confirmed by endoscopic retrograde cholangiography with sphincterotomy and/or by surgery; negative findings were confirmed by clinical follow-up. The accuracy of EUS findings were confirmed as follows: 237 true-positive, 216 true-negative, 2 false-positive, 4 false-negative, 4 incomplete (sensitivity 98%, specificity 99%, positive predictive value 99%, negative predictive value 98%, accuracy 97%). In 214 (46%) patients, more invasive investigations were avoided. The mean cost for patients managed by the EUS-based strategy was significantly less than the theoretical mean cost of patients undergoing endoscopic retrograde cholangiography.

This study confirms that EUS is highly reliable for the diagnosis of choledocholithiasis which has been shown in many studies however. What is more important is that the authors showed that EUS as the first test for choledocholithiasis may offer important clinical and economic advantages by preventing ERCP induced pancreatitis and other complications in patients without significant findings in the bile duct on EUS.

§ Fritscher-Ravens A, Bobuslavizki KH, Brandt L, Bobrowski C, Lund C, Knoefel WT, Pforte A. Mediastinal lymph node involvement in potentially resectable lung...
This is a prospective comparison of thoracic CT, Positron emission tomography (PET), and endoscopic ultrasonography (EUS) with fine needle aspiration (FNA) for detection of lymph nodes metastases in patients with lung cancer. After bronchoscopic evaluation, CT, PET, and EUS were performed to evaluate potential mediastinal involvement in 33 consecutive patients with bronchoscopic biopsy/cytology proven (n = 25) or radiologically suspected (n = 8) lung cancer with surgical histology as “gold standard”. CT, PET, and EUS detected mediastinal lymph nodes in 15, 14, and 27 patients (21 of which were suspected to be malignant on EUS), respectively. For correct prediction of mediastinal lymph node stage, the sensitivities of CT, PET, and EUS were 57%, 73%, and 94% with specificities of 74%, 83%, and 71%; accuracies were 67%, 79%, and 82%. Results of PET could be improved when combined with CT (sensitivity, 81%; specificity, 94%; accuracy, 88%). The specificity of EUS (71%) was improved to 100% by FNA cytology (EUS-guided FNA).

No single imaging method alone could be considered conclusive in evaluating potential mediastinal involvement in apparently operable lung cancer under routine clinical care. A tissue diagnosis is extremely helpful and EUS with FNA combination emerged as the most useful technique in the evaluation of even very small mediastinal metastases of lung cancer. CT seems necessary additionally to evaluate the pretracheal region as well as the rest of the thorax, and PET may be valuable to detect distant metastases.

This is a well done study comparing three imaging modalities described above in a prospective fashion. This study helps clarify some of the concepts about where each of the three staging modalities—i.e. CT, EUS, and PET—stand if all three were easily available at an institution for staging of operable lung cancer. As shown here, these imaging modalities have their pros and cons, but one cannot claim any one of them as a complete replacement for the other. Rather, if all three are available, they may be complementary rather than competitive. However, when “tissue is the issue,” EUS clearly is the way to go among them due to its ability to direct FNA in a safe, minimally invasive fashion.

Technical Updates || David Rubinstein, M.D. & Karl Reimig, Ph.D.

Tips for Using the Visible Human Interactive Atlas

One of the unique features of VHJOE is the many links to the Visible Human Interactive Atlas (VHIA). This tool is a powerful resource, enabling physicians to reference actual planar anatomy that correlates to diagnostic images. A tutorial with basic instructions for using the Atlas can be found at http://visiblehumanexperience.com/oblique-maker/tutorial.asp. This column provides additional information about the Atlas, as well as, advanced tips for using the VHIA.

The VHIA will run on computers running either Windows or Macintosh operating systems. The Atlas will function slightly differently on the Macintosh operating system since it uses a one button mouse. Differences will be explained in the sections that follow.

The first step in using the VHIA is to install the software that is necessary to run it. The VHIA is a Java applet, a program written in the Java programming language that usually runs in a web browser and cannot read from or write to your hard drive. Java is a part of most web browsers or is included in the operating system of most personal computers and usually does not have to be installed. The use of interactive 3-dimensional models to navigate through the Visible Human data necessitates additional software, GL4Java. This software can be installed on PCs from http://visiblehumanexperience.com. You may register for free at the website. The registration requires giving your name and email address but is not used to send emails. Then mouse over the words “Oblique Maker” and choose install from the drop down menu. Macintosh and PC users can also download the software at the GL4Java website (http://www.jausoft.com/products/g4java/g4java_install.html).

To install the software, one must have administrator privileges on the computer. One usually has these privileges on a personally owned computer but may not on institutional computers.

Once GL4Java is installed the VHIA can be used. The basic instructions can be read by pressing the “HELP” button, which is located on the left side of the tools window. This will also provide a link to the tutorial. There are many features that are not explained in the basic instructions or tutorial.

Using the Mouse in the 3D Window

Take a look at the Tools window shown in Figure 1. The combination “Drag the Mouse to…” and “Type of Motion” determines what will move and how the mouse motion with the left button depressed will affect its movement. For example, with the “Move Image Plane” selected for the “Drag the Mouse to…” and the “Move Horiz./Vert.” selected for the “Type of Motion”, as shown here, dragging with the left mouse button depressed will cause the image plane to move across the screen.

To get the image plane to rotate with the left mouse button, you could change the “Type of Motion” to “Rotate.” Then dragging using the left mouse button would cause the image plane to rotate about its center. However, you can also get the image plane to rotate by pressing the right mouse button and dragging. In addition, pressing the right and middle buttons simultaneously and dragging will cause the image plane to move in and out of the screen. It is possible to achieve any desired image plane position and orientation by using combinations of the left, middle, and right buttons. This makes positioning and orienting the image plane far faster and easier than continually altering the “Type of Motion” option and using only the left mouse.

To move the models, including the image plane, select “Move All Models” as the option for “Drag the Mouse to…” Note that with the cursor in the 3-D model window, you can toggle between the choices of “Move Image Plane” and “Move All Models” by simply double clicking the left mouse button. Then dragging with the right button will rotate the models, dragging with the middle button will pan the models, and dragging with the middle and right button will translate the models.
buttons will cause the models to move in and out of the screen. Dragging with the left button will cause the models to do whatever is selected as the “Type of Motion.”

Pressing keys can also alter the function of the mouse on both PCs and Macs. Pressing the alt key (option on a Mac) and the left mouse button does the same thing as pressing the center mouse button. Pressing the shift key and left mouse button is the equivalent to pressing the center and right mouse buttons. Pressing the control key and the left mouse button is the same as pressing the right and left mouse buttons. On the Mac, the command key will mimic the right mouse button on a PC.

Orientation in the 3D Window

There are two tools to aid in orientation in the 3D window, Blockhead in the upper right corner of the window and the colored image plane (Figure 2).

Blockhead serves as a compass to indicate the directions the overall view has been rotated. The view of Blockhead corresponds to the orientation of the models. If you are viewing Blockhead from behind, you are also viewing the models from behind.

The image plane in the 3D window represents the space occupied by the generated anatomic image. It has red and blue markers that correspond to the orientation of the anatomic slice. The large blue rectangle corresponds to the top of the image as you would view it and wraps onto the top edge of the plane. The large red rectangle corresponds to the bottom of the image as viewed from behind the image and wraps onto the bottom edge of the plane. The edge of the plane that corresponds to the right side of the anatomic image has a small red marker in the center and the edge that corresponds to the left side has a blue marker.

Using the Mouse Buttons in the Oblique Window

Dragging the mouse in the oblique window will allow you to measure objects. A double click will toggle on and off the labels of structures as an overlay on the anatomic image. If the labels are off, the name will appear in the title bar of the window and measurements will appear as an overlay. If the labels are on, the measurement will appear in the title bar.

New Features

Originally, the planar anatomic image in the oblique window was generated by clicking a button. It is now automatically retrieved when the mouse drag is completed.

The image plane can now be moved in steps perpendicular to the plane. Pressing the “STEP +” button in the Tools window will move the plane a small increment in the direction of the side with the large blue rectangle. (See Figure 3.) The “STEP −” button will move the plane a small increment in the opposite direction. (See Figure 3.) If “Move Plane” is selected, dragging with the left, right, and center mouse buttons simultaneously depressed while in the 3-D models window will move the plane along an axis perpendicular to the plane. Dragging with left button and the shift and alt (option) keys pressed will do the same.

To move the image plane in a direction parallel to the plane, drag the mouse with the center mouse button pressed in the “Oblique Section” window. This will also move the anatomic image in the “Oblique Section” window. The same action can be achieved by dragging with the left mouse button pressed while the alt (option) key is pressed.

To ensure the newest features are working on your computer, you should delete the temporary internet files or browser cache. On Internet Explorer, choose “Internet Options…” from the “Tools” menu. Then, choose the “General” tab and push the “Delete Files…” button in the Temporary Internet files section.

Saving Your Work

The entire state of the VHIA can be saved in two ways by clicking the “SAVE STATE” button in the Tools window. As shown in Figure 4, a new browser window will open with a page that says “SAVE THIS PAGE AS AN HTML PAGE OR BOOKMARK.” By choosing “Add to Favorites …” in the “Favorites” menu on Internet Explorer, the state can be saved as a favorite or bookmark. Choosing this favorite at a later time will restart the VHIA applet with the same models in the same position and with the same anatomic image as when the state was saved.

By choosing “Save as …” from the “File” menu on Internet Explorer and then saving as a webpage, a file can be saved. Opening this file at a later time will open the VHIA applet in the saved state.

The planar anatomic image can be saved by itself as a JPEG image. This is done simply by clicking the “SAVE JPEG” button in the Tools window. A new browser will open with the single image in it. The image can be saved by right clicking on the image or choosing “Save as …” from the “File” menu.
Featured Movie || John C. Deutsch, M.D.

Visible Human: Thorax in Radial Echo Endoscopic Orientation

This month we are featuring a Visible Human movie of the thorax made in an orientation that one would see using a radial echo endoscope. As usual, there is a labeled image (Figure 1) to orient one to the beginning of the movie, and there is a link to the Visible Human database [online only]. We have also included an audio descriptor that accompanies the movie as it plays. We hope you find these features both interesting and useful.

Figure 1: Labelled image as starting point to Video Clip 1.

Video Clip 1: Radial echo endoscopic view of the thorax of Visible Human data.