

Applying JMP®'s Imaging Analytic Tools to Target Prostate Cancer Tumors that Guide External-Beam Radiation Therapy

Melvin Alexander, Social Security Administration

ABSTRACT

The motivation of this paper came from questions I received on my SESUG 2016 presentation. There, I showed how John Ponte's JMP Image Column Analyzer add-in could select frames of MRI prostate cancer images (saved in an Expressions column). The selected frames showed special markers near the prostate. These markers identified the location where to aim radiation beams that will kill the cancer cells without harming healthy cells. Selected frames with the markers were output to JMP data tables representing the image data. I appended the marker-frame data tables into a larger JMP data table.

In this presentation, I compute kernel density estimates (non-parametric measures) of the marker's intensity values from the Bivariate Analysis >Nonpar Density platform. Contour lines with the largest density of marker's intensity values provide useful metrics for further data analysis and exploration.

INTRODUCTION

This presentation applies medical imaging analytics techniques in targeting prostate cancer tumors for external-beam radiation therapy (EBRT). The motivation for this presentation came from questions raised during a paper I delivered at the SESUG 2016 conference, Alexander[1]. There, I demonstrated JMP's graphical capabilities in converting pixel values from images recorded from ultrasound, computer tomography (CT), and magnetic resonance imaging (MRI) technologies. These images were converted into data tables and matrices. Once data are in data tables, additional analyses and data visualizations may be performed. Results of the image analyses can help medical clinicians (urologists and oncologists) find the precise location of the prostate to aim radiation beams that can kill cancerous cells and avoid hitting noncancerous cells. This topic has sparked a lot of interest among radiologists I worked with in the Department of Diagnostic Radiology at the University of Maryland Medical Center (UMMC) and Sinai hospital in Baltimore. Radiologists are MDs who use ultrasound, computer tomography (CT), and magnetic resonance imaging (MRI) technologies in the diagnosis and treatment of patients with traumatic injuries and medical disorders.

Combining the statistical, graphic, and data analytic functionality of JMP® extends information visualization beyond what can be seen with standard image interpretation.

This presentation will use JMP® Image Column Analyzer to output MRI prostate cancer images (stored as an Expressions column) into distinct data tables. The output Data Tables show the placement of fiducial (gold) markers that precisely locate prostate cancer tumors. These markers help radiation oncologists know where to aim radiation doses that kill tumors without harming healthy cells.

Next, I will compute non-parametric probability density estimates of fiducial marker intensity values. Values of these fiducial -marker intensities uniquely distinguishes them from other objects that have close-but-different intensity values. These estimates are important for establishing tolerance measures for fiducial marker identification with high degrees of confidence in future applications.

BACKGROUND

The prostate is a walnut-sized organ that sits in the pelvic area, below the bladder, and surrounds the urethra (which passes urine from the bladder). Prostate cancer is slow growing and disrupts the urinary and erectile functions, mostly in males over 40 years old. Estimated deaths this year are about 29,000 and are much lower than 15 years ago due to great advances in diagnoses and treatments. Prostate cancer is detected by drawing blood to measure Prostate Specific Antigen (PSA) levels (normal levels are below 4 ng/mL).

PSA levels 2.5-3 times above the 4 ng/mL limit are followed by taking biopsy samples of prostate tissues to determine the amount and aggressiveness of tumorous cells present. If biopsy results reveals serious cancer-cell growth, then treatments options such as medicine, surgery, or radiation therapy are discussed with the patient. For elected radiation-beam therapy (which tends to have faster recovery times with fewer side effects than medicine or surgery), fiducial markers ("seeds") are inserted into prostate sections. Fiducial markers help the treatment team locate the site where radiation beams target tumors without harming healthy cells.

Panel 1a of Figure 1 shows the relative size of a fiducial marker (usually made of gold, carbon, or polymer) that are approximately 0.3 mm in diameter and 1.0 mm long. One can compare the relative size of a fiducial marker with a match stick. Panel 1b illustrates how fiducials are inserted into the prostate using sterilized gauge needles. They are inserted into the prostate by a board-certified urologist guided by the use of ultrasound imaging. Fiducials are

generally a standard, preliminary step before administering Radiation Beam Therapy (RBT). Subsequently, the radiation oncologist will examine fiducials during MRI examination before administering daily treatments. Fiducials appear as small "light" dots (or bullet-shaped seeds) on MRI image frames that generally do not need to be removed following treatment.

Figure 1: Example Illustrating the relative size and insertion of Fiducial Markers into the Prostate. Sources:
<http://goodhealthlifand.blogspot.com/2015/05/good-prostate-health-tips.html>,
<http://www.wienkav.at/kav/kfj/91033454/physik/images/Acculoc-and-ab-medica.png>

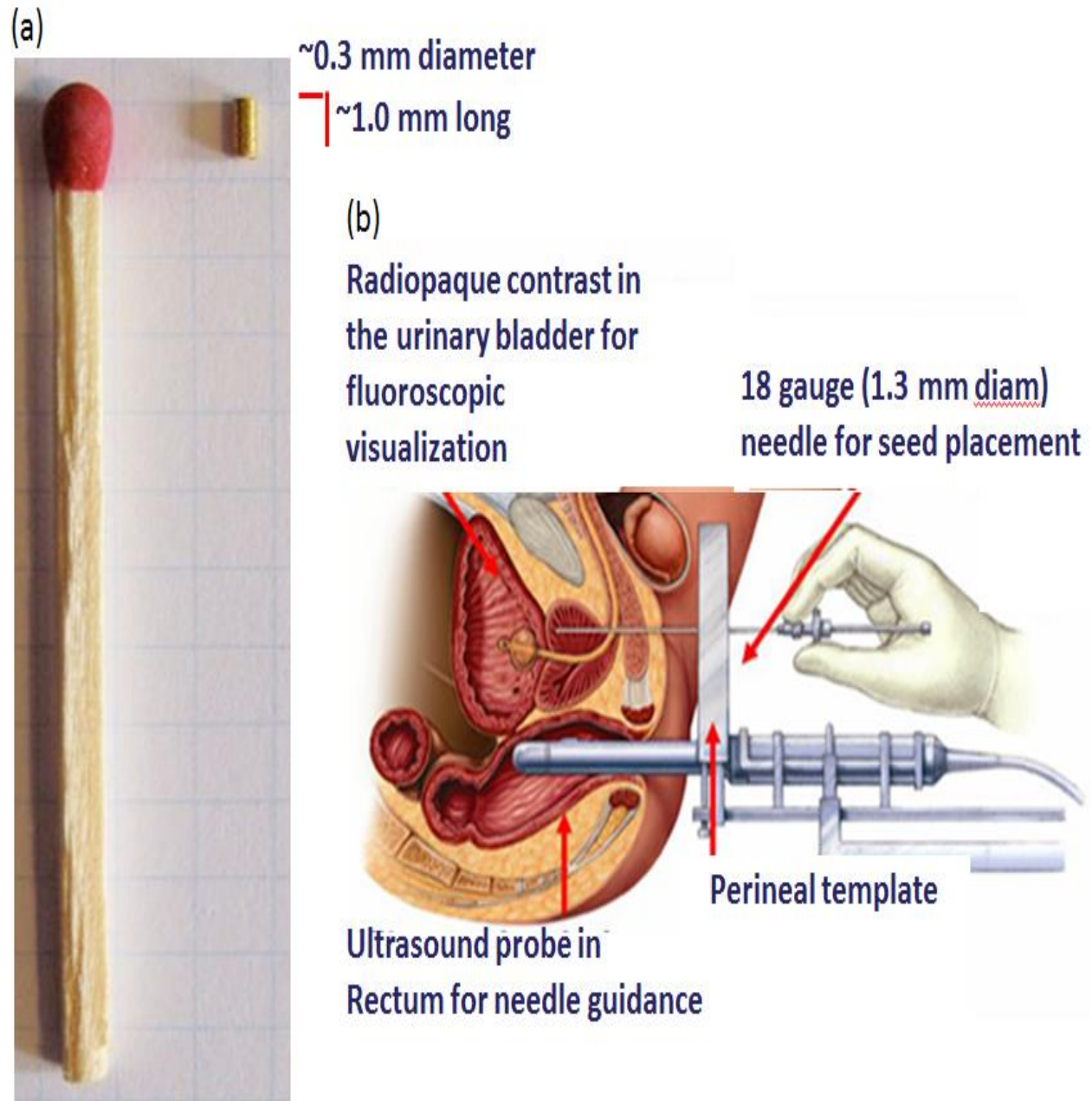
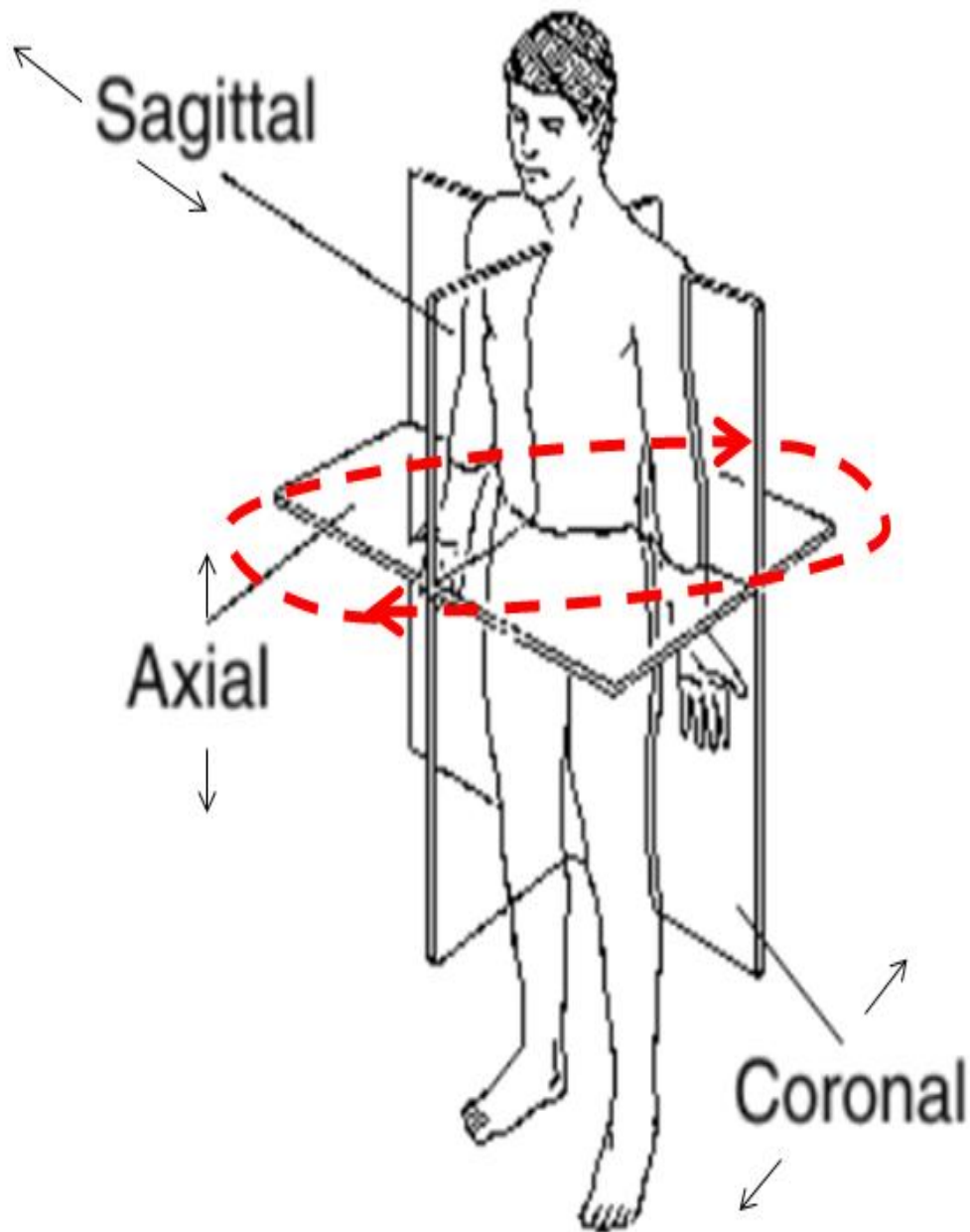


Figure 2(a) shows the three-dimensional anatomical planes (axial, coronal, and sagittal) where cross-sectional body slices are recorded during CT or MRI imaging. Figure 2(b) depicts the MRI scanning process.

Figure 2a: Anatomical Planes that capture image frames of MRI scans

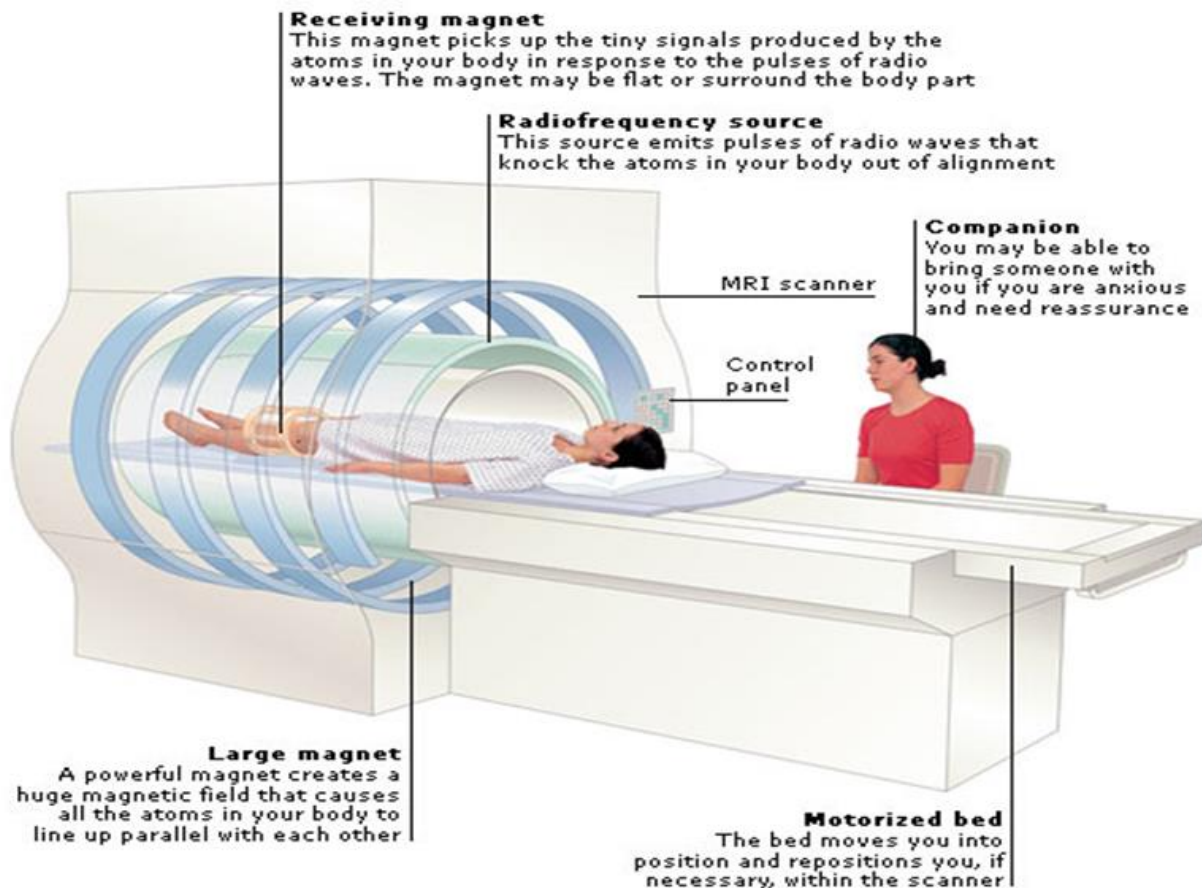
Sources: (a) <http://webdocs.cs.ualberta.ca/~btap/Images/planes-body.gif>



The axial (or transversal) plane is recorded from top-down (head-to-toe). The Coronal plane captures the body from front-to-back. The Sagittal scans the body from the left-to-right shoulder. The elliptical pattern represents the cross-sectional body frame captured in the scanning process. Each image frame depicts the body organ's structure, location, direction, and movement.

Figure 2b: Illustration of the MRI scanning Process

Source: <http://www.aviva.co.uk/health-insurance/home-of-health/medical-centre/medical-encyclopedia/entry/procedure-having-an-mri-scan/>



Typically a patient lies on a table that slides through a tunnel (Figure 2b). A receiving magnet takes radio frequency-wave signals of re-aligned atoms in the body. The radio wave signals are converted into image scans of the cross-sectional slice of the body as the patient moves through the tunnel of the scanner. Several cross-sectional image scans are taken during the procedure. The patient lies still within the scanner for about 10 minutes, each frame is taken about 30 seconds apart. Patients may wear earplugs or headphones because the scanner can be noisy. The cross-sectional images generated from the MRI scan are reformatted. These images are viewed on a computer monitor, printed on film; transferred to a CD or DVD; and stored into a Picture Archival Communication System (PACS). Bones appear white on the MRI. Soft tissue organs like the heart, bladder, or liver shows up in shades of gray. Air appears black. Fiducials look like "white" dots or seeds on image frames.

Figure 3 uses the Image Column Analyzer add-in, Ponte [2], to open images stored as expression columns in a JMP data table (Hales, [7, 9] and Nelson [8]). Expressions columns allow pictures, matrices, lists, and other objects to be added to JMP data tables. When the **Create Data Table** button is clicked, a data table representing the image data is created. The new data table name has a new column with the row number read from the original JMP data table. This feature is useful whenever multiple CT image frames of the same body region/section (or anatomical plane) were saved in rows of the data table. This way, multiple data tables of each image can be generated that tell which frame the images come from.

The following JSL script can create a new data table with images added to an expressions column:

```
/******
```

References

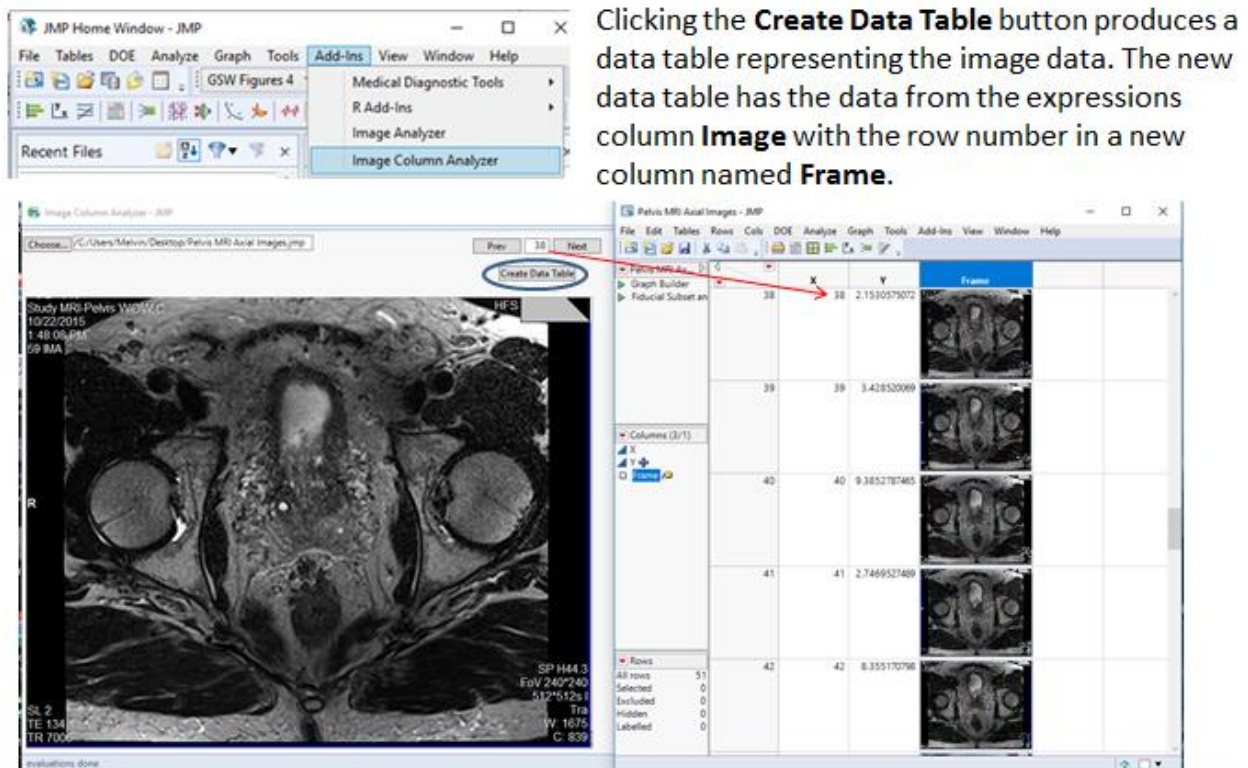
- (1) Jim Nelson, 12Oct2016, "Re: Crop Image and Insert Crop Into Data Table", <https://community.jmp.com/message/231311#231311>

```
(2) Craige Hales, 07Oct2016, "Importing Several .jpg files into a
Expression Column",
https://community.jmp.com/message/231214#231214,
(3) M. Sharp, 25Apr2017, "Import Image from URL into Expression Column",
https://community.jmp.com/t5/Discussions/Import-Image-from-URL-into-Expression-Column/m-p/15922#M14546
(4) M.Anderson, 15June2017, "Adding Images to A Data Table From a Directory",
https://community.jmp.com/t5/JMP-Scripts/Adding-Images-to-A-Data-Table-From-a-Directory/ta-p/40341

*****/
//location where images are stored
path = "G:\Nitima\Manuscript draft\pics\" ;
pic = filesindirectory(path) ;
/* New data table ("Pelvis MRI Axial Images") has columns, name of the image stored
in the pics folder and the imported image (image) */

dt = New Table("Pelvis MRI Axial Images", Add Rows(N Items (pic)),
    New Column("Pelvis MRI Axial Images", Character, Nominal, Set Values
        (pic)),
    New Column("Image", Expression, Formula(New Image(dt:Location||:Pelvis MRI
Axial Images)))) ;
dt << Set Table Variable("Location",path);
```

Figure 3: Example using Image Column Analyzer add-in to open images stored in an expression column of a JMP data table. Source: Ponte (2016), <https://community.jmp.com/docs/DOC-9901>



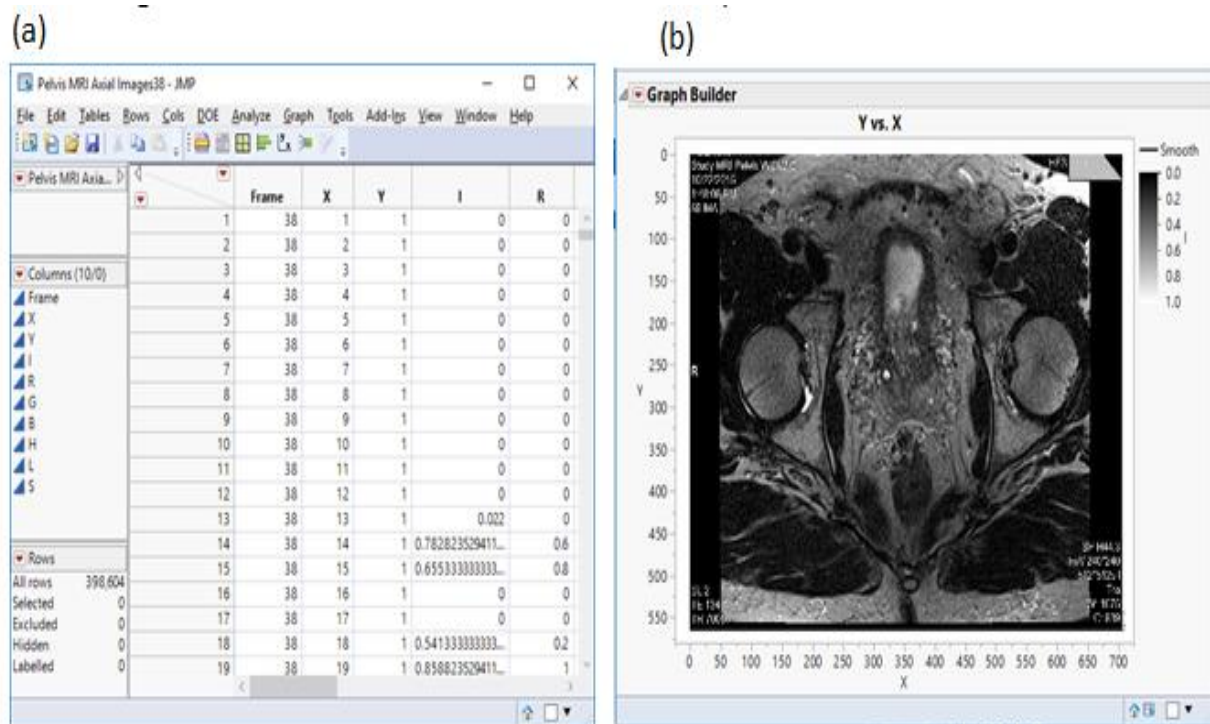
This way, multiple data tables may be generated from different images so that one can tell which one is which.

Figure 4(a) displays the data table of pixel coordinates and red, green, blue (RGB) colors that are transformed into hue, lightness, saturation (HLS) colors and grey-scale intensity (I) values. In other words, the data table gives a

numerical representation of the image shown on the right in Figure 4(b) using JMP's Graph Builder. The following JSL commands also produced the Graph Builder display of Figure 4(b):

```
//JSL code to produce Graph Builder plot of Image in panel (b)
Graph Builder( Size( 579, 500 ), Variables( X( :X ), Y( :Y ), Color( :I ) ),
Elements( Smoother( X, Y, Legend( 3 ) ), Points( X, Y, Legend( 4 ) ) ),
SendToReport( Dispatch( {}, "Y", ScaleBox, {Reversed Scale} ),
Dispatch( {}, "400", ScaleBox, {Legend Model( 4, Properties( 0,
{gradient({Color Theme( "White to Black" ), Reverse Labels( 1 )})}
) } ) ) );
```

Figure 4: Selected Records of the Data and Graph Builder Plot of Frame 38

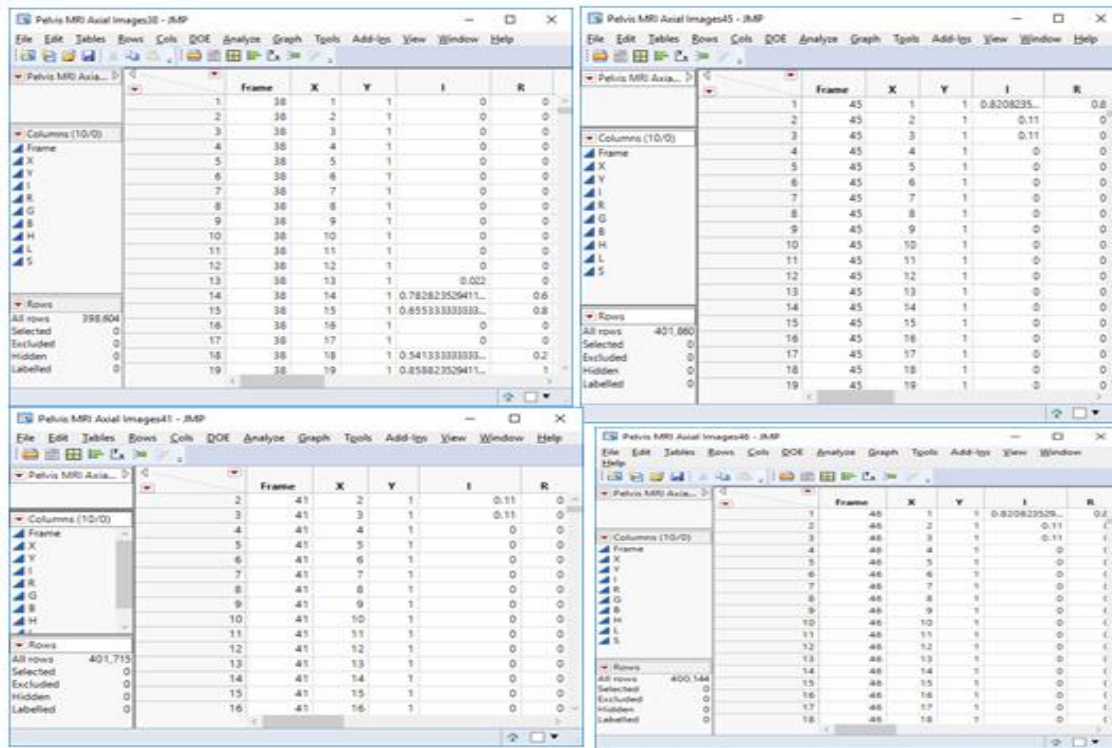


To manually reconstruct the plot of Figure 4(b) from the active data table in Figure 4(a), do the following steps:

1. Launch Graph Builder (**Graph > Graph Builder**)
2. Drag and Drop the **X** and **Y** columns into the X and Y axis drop zones, respectively
3. Select the **Points** element icon
4. Double-click the **Y** axis and check the **Reverse Order** box
5. Drag and Drop column **I** into the **Color** drop zone
6. Right-click the **Legend** scale (**Smooth**)
7. Select **Gradient**
8. Change the color theme to **Sequential**
9. Check the **Reverse Scale** box to flip the color values so that they match the original image
10. Click **OK** to apply the settings to the plot.

Multiple Data Tables (Frames 38, 41, 45, and 46 of the MRI Axial Pelvis images) in Figure 5 are output after clicking the **Create Data Table** button of the Image Column Analyzer.

Figure 5: Image Data Tables of Frames 38, 41, 45, and 46.



Dialog screens append the four data tables shown in Figure 5 to form a single combined data table with the **Table > Concatenate** platform or JSL script as shown in the upper and lower panels of Figure 6.

Figure 6: Dialog Screens that appends the 4 data tables of Figure 5 to form one-combined data table

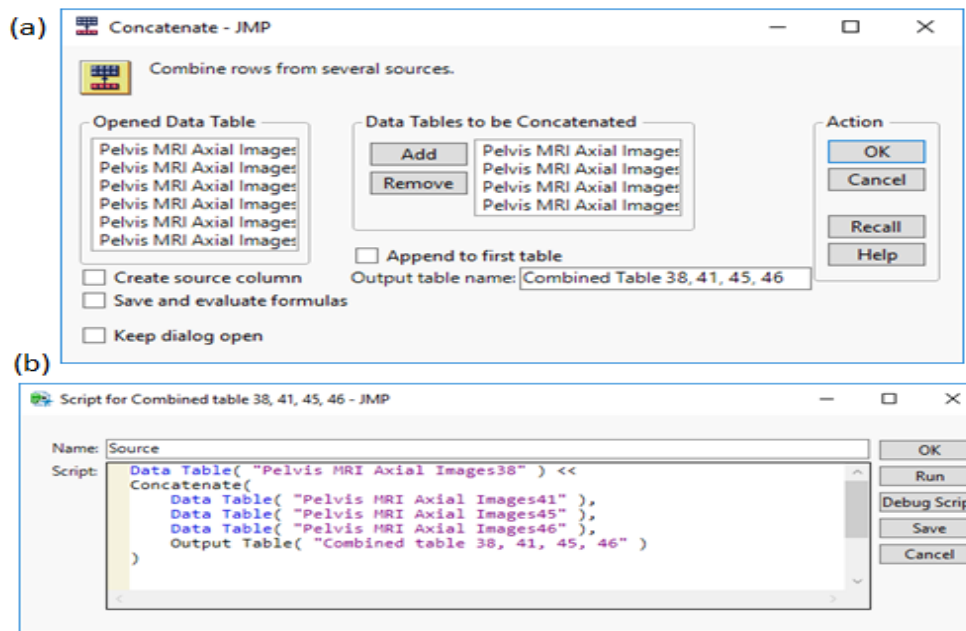


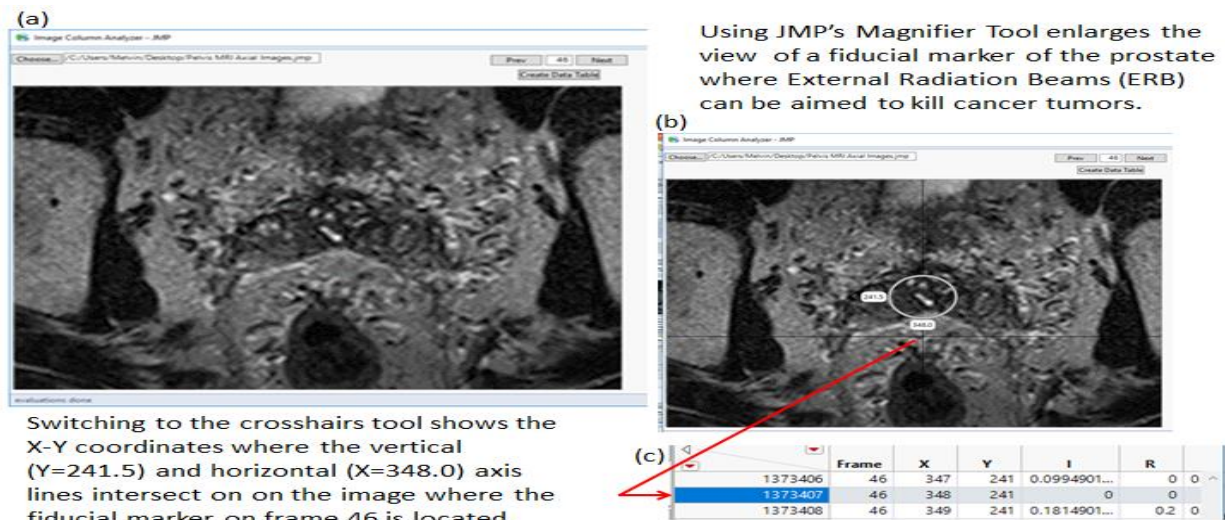
Figure 7 shows a portion of the combined data tables (Frames 38, 41, 45, and 46) of the MRI Axial Pelvis images with over 1.6 million rows.

Figure 7: Screen appending the 4 data tables of frames 38, 41, 45, and 46.

	Frame	X	Y	I	R	G	B	H	L	S
1	38	1	1	0						
2	38	2	1	0						
3	38	3	1	0						
4	38	4	1	0						
5	38	5	1	0						
6	38	6	1	0						
7	38	7	1	0						
8	38	8	1	0						
9	38	9	1	0						
10	38	10	1	0						
11	38	11	1	0						
12	38	12	1	0						
13	38	13	1	0.022						
14	38	14	1	0.7828235...						
15	38	15	1	0.6553333...						
16	38	16	1	0						
17	38	17	1	0						
18	38	18	1	0.5413333...						
19	38	19	1	0.8588235...						
20	38	20	1	0.06						

Figure 8(a) shows the fiducial marker of frame 46. The Magnifier tool in Figure 8(b) allows the user to zoom in on an image frame to enlarge the view of the prostate area where the fiducial marker was placed. Hitting the letter “C” switches to the crosshairs tool. Hovering the pointer over the fiducial and clicking the left-mouse button shows the X-Y coordinates where the axis lines intersect. Here, the X-Y coordinates are X=348, Y=241, which corresponds to the selected row of the combined data table shown in Figure 8(c).

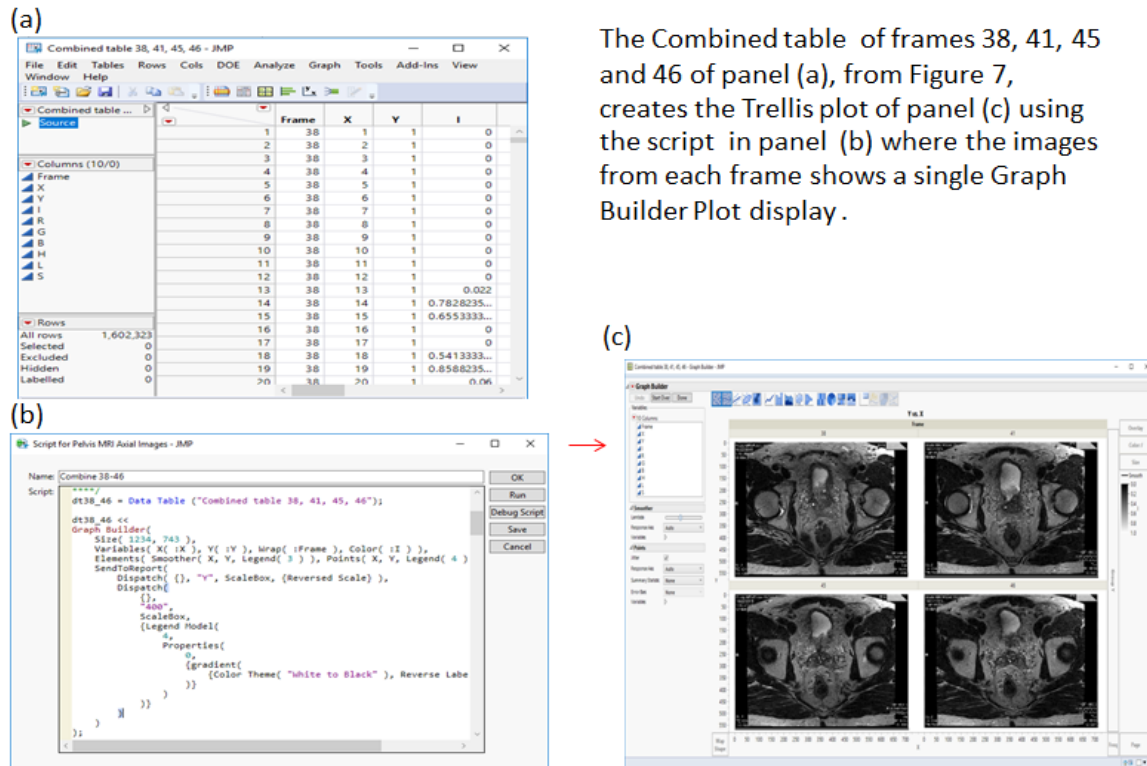
Figure 8: Image Data Output of Frame 46.



Multiple Data Tables output from clicking the **Create Data Table** button may be appended together to form the Trellis plot in Figure 9(c) from the data table and JSL script of Figures 9(a) and 9(b). Panel 9c shows the oncologist and treatment team where the fiducial markers were placed as a preparatory step before the patients undergoes radiation

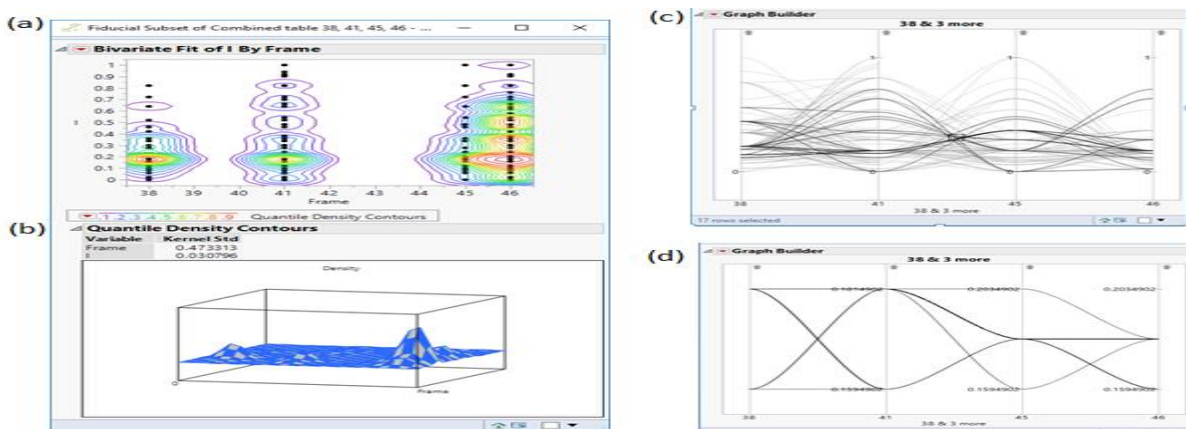
treatment. The patient will then have additional CT and MRI scanning to model the precise locations of the targeted cancerous cells. Tattoos are marked on each hip and the pubic regions of the patient. These tattoos serve as landmarks for achieving accurate, consistent treatment during radiation beam therapy. In order to obtain useful metrics of fiducial markers from the image frames, we select the intensity column as the measure of interest.

Figure 9: Image Data from Figure 7 with JSL script that create Trellis plots of Frames 38, 41, 45, and 46.



JMP's Bivariate Fit Y by X platform is used to find the fiducial intensity values across the saved, selected frames. The Non par (non-parametric) option produces contour lines showing the density of fiducial intensity values shown in Figure 10. The peak contour plot in Figure 10(a) contains 95% of the intensity values. In other words, the intensities in the innermost Quantile Density Contours are the strongest values that quantify the fiducial intensities from the various axial cross-sectional slices of the prostate. The intensities were important for the oncologist and treatment team in finding the sites to aim radiation beams.

Figure 10: Contour, 3D Mesh, and Parallel Coordinates Plots from the Fiducial Subset JMP data table



The Mesh plot of Figure 10(b) give a three-dimensional plot of the fiducial intensities over a grid of image frames 38, 41, 45, and 46. The parallel coordinates plots in Figures 10(c) and 10(d) show that most of the fiducials have specification limit endpoints between 0.15 and 0.20. The intensity values of Figures 11(a) and 11(b) serve as a first step in establishing quantitative tolerances (a.k.a. reference centroid values or rcvs) that estimate what the “true” intensity values for fiducials should be. The use of the Reference Centroid Values applied in this case study is similar in approach to the use of these values in identifying cheetahs by Wild Track [3].

Figure 11: Fiducial Marker Intensity Tolerance Value for Figure 10(c) and Variability Gauge Chart.

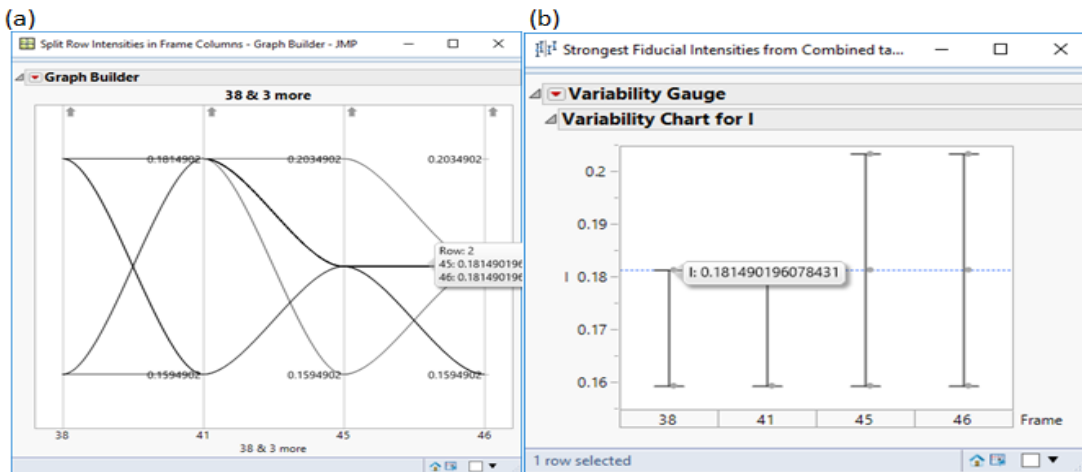
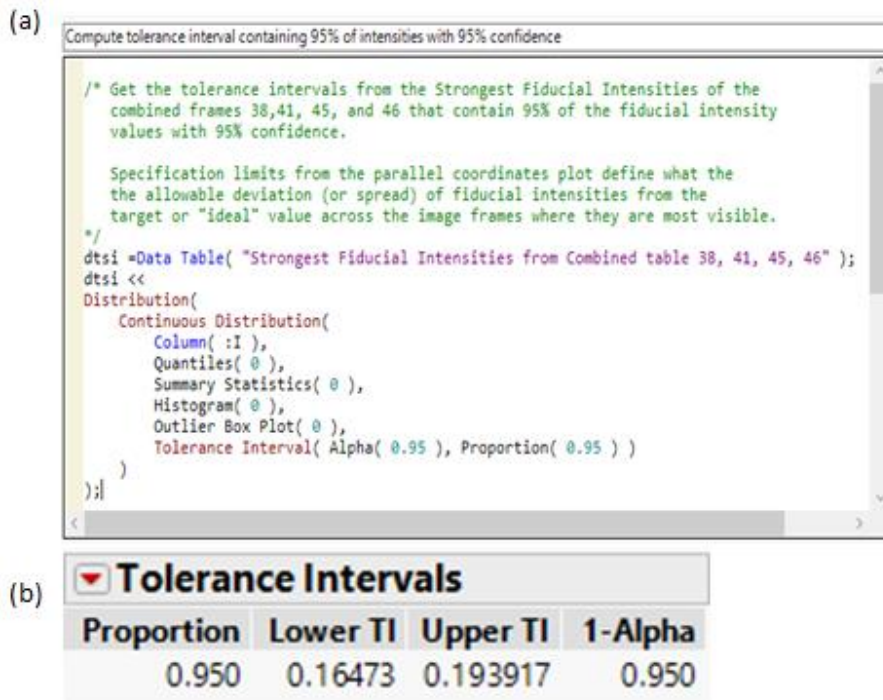


Figure 12(b) shows the Tolerance interval containing the 95% of the fiducial intensity values with the specified probability of 95% using the JSL script in Figure 12(a).

Figure 12: Tolerance Interval containing 95% of the Fiducial Intensity Values with a Probability of 95%.



The tolerance interval (0.165, 0.194) of Figure 12(b) lies within the specification spread (0.159, 0.204). This suggests that the fiducial marker intensity values are reasonably realistic.

SUMMARY AND CONCLUSIONS

This case study patient completed External Radiation Beam Therapy (ERBT) over an 8-week period. Follow-up visits with the patient's urologist and oncologist revealed PSA levels that were within normal ranges (below 4 ng/mL). The patient had PSA – level tests every six months and continues to make progress after EBRT. JMP's Imaging Analytic Tools are charting new territory for medical imaging that extends to broader computer-vision applications such as object recognition, and identification used in medical diagnosis and treatment.

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CONTACT INFORMATION

Your comments and questions are valued and encouraged. Contact the author at:

Melvin Alexander
Social Security Administration
6401 Security Blvd.; East High Rise Building (4-A-6)
Baltimore, MD 21235
Phone: (410) 966-2155
Fax: (410) 597-0354
E-mail: Melvin.Alexander@ssa.gov

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