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Prospective clinical implementation of a novel MR-tracking device for real-time HDR brachytherapy catheter positioning

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Abstract

Purpose—We designed and built dedicated active MR-tracked (MRTR) stylets. We explored the role of MRTR in a prospective clinical trial.

Methods and materials—Eleven gynecologic cancer patients underwent MRTR to rapidly optimize interstitial catheter placement. MRTR catheter tip location and orientation were computed and overlaid on images displayed on in-room monitors at rates of 6–16 frames-per-second. Three modes of *actively-tracked* navigation were analyzed: *coarse navigation* to the approximate region around the tumor; *fine-tuning*, bringing the stylets to the desired location; *pull-back*, with MRTR stylets rapidly withdrawn from within the catheters, providing catheter trajectories for radiation treatment planning (RTP).

Procedure—Catheters with conventional stylets were inserted, forming baseline locations. MRTR stylets were substituted, and catheter navigation was performed by a clinician working inside the MRI bore, utilizing monitor feedback.

Results—*Coarse navigation* allowed repositioning of the MRTR catheters tips by 16 mm (mean), relative to baseline, in 14 ± 5 s/catheter (mean $\pm$ std). *The fine-tuning mode* repositioned the catheter tips by a further 12 mm, in 24 ± 17 s/catheter. *Pull-back mode* provided catheter trajectories with RTP point-resolution of ~ 1.5 mm, in 1–9 s/catheter.

Conclusions—MRTR-based navigation resulted in rapid and optimal placement of interstitial brachytherapy catheters. Catheters were repositioned compared to the initial insertion without

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tracking. In pull-back mode, catheter trajectories matched CT-precision, enabling utilization for RTP.

Introduction

For the precise delivery of radiation therapy, magnetic resonance imaging (MRI) guidance has been shown to provide improved delineation of the target tumor and surrounding viable tissues. An additional MRI advantage, compared to CT imaging, is the lack of exposure to ionizing radiation, as well as use of non-ionic contrast agents. The utilization of MR in radiation oncology has increased in the past 10 years due to the implementation of MR simulators [1] and MR-based radiation treatment [2]. MR-guided gynecologic interstitial brachytherapy was first tested in the U.S. in a prospective trial initiated in 2004 [3, 4]. Insertion of brachytherapy applicators and stylets under MR guidance for gynecologic brachytherapy treatment is an active field of investigation [5].

High Dose Rate (HDR) brachytherapy catheters are made of flexible hollow plastic tubes with a sealed tip, into which a high-activity radioactive source is robotically driven to achieve the desired dose distribution. To provide the mechanical strength needed to traverse soft tissue, a semi-rigid tungsten alloy needle (“stylet”) is inserted into the plastic tube at the time of catheter implantation, to drive the catheter from the skin entry-point to the target location. Therefore, a reliable and rapid tracking of the stylet’s instantaneous location during insertion is crucial to the temporal efficiency of the procedure, as well as to closer agreement between the desired catheter locations and their final position at the end of the insertion process. In addition, the final catheter spatial trajectories need to be accurately defined, in order to perform radiation treatment planning (RTP) that will lead to optimized administration of dose, which will provide for successful outcomes (i.e., reduced toxicity, lower recurrence rate) of HDR brachytherapy procedures.

MRI-guided HDR brachytherapy catheter insertion provides excellent tumor and surrounding-tissue visualization. However, to date, all real-time MR based catheter insertion has utilized passive tracking. Passive tracking, which utilizes magnetic susceptibility artefacts produced by metallic objects on MR images, has been used in brachytherapy for navigating stylets to the target [6], as well as for RTP at the end of catheter placement. The susceptibility artefacts depend on the device’s shape and material properties, its orientation relative to the static magnetic field (B_0), as well as specific MRI pulse sequence parameters (e.g., TE, spatial resolution, pixel bandwidth) [7]. Passive MRI tracking suffers from deficiencies relative to CT-based localization; long (>1min) scans are required to find the stylet, image artefacts are generally larger than the physical stylet size, leading to lower spatial resolution localization, and the artefacts may not be centered on the physical device, leading to errors in catheter location and orientation. In addition, with passive tracking, it is difficult to separate between multiple catheters, especially when their paths approach or cross each other. Due to the inaccuracy of MRI passive tracking, common practice is to require marker placement in order to identify the catheter location, and more commonly to perform CT catheter localization after the MRI insertion procedure.

Active MR-tracking (MRTR) is a method developed for endo-vascular navigation of non-metallic catheters in the 1990s. MRTR is achieved by mounting radio-frequency (RF) micro-coils on the tracked device, and employing a specific MRI pulse sequence, which generates the precise (sub-mm resolution) location of the micro-coils along the X (left-right), Y (anterior-posterior), and Z (head-foot) directions, within ~40 milliseconds [8–10]. We recently introduced MRTR into radiation oncology. The method required substantial revision, since for navigating brachytherapy stylets, the MR-tracking coils must be placed on the shaft of metallic devices. Active tracking of metallic devices is challenging because of static (B_0) and RF (B_1) magnetic field in-homogeneities, which are exacerbated by close proximity of multiple stylets. These problems were resolved by use of novel RF coil geometries and improvements in the MR-tracking pulse sequence [11, 12].

For clinical implementation, MR-tracked stylets were constructed utilizing two flexible printed circuit (FPC) RF micro-coils, mounted on the distal end of the metallic stylet, and connected to individual MRI receiver channels. Detailed device technical description is available [11]. As noted in our prior study, the MRTR technique improved stylet localization resolution to $\sim 0.6 \times 0.6 \times 0.6 \text{ mm}^3$, relative to passive tracking, whose resolution is $\sim 3 \times 3 \times 3 \text{ mm}^3$, and also improved the tracking frame rate to 6–16 Hz, relative to $\sim 0.4 \text{ Hz}$ [12].

We report on the results of application of MRTR to HDR interstitial brachytherapy catheter insertion in eleven gynecologic cancer patients enrolled in a prospective clinical trial. We quantified the clinical performance of the procedure, gauging its safety, as well as the positional accuracy and speed of catheter insertion, relative to initial insertion with passively-tracked MRI practice and CT-based HDR brachytherapy.

Methods

Patients and catheter navigation procedures

With an institutionally-approved IRB protocol, a prospective trial of MRTR was conducted for catheter placement in 11 gynecologic cancer patients with complex tumors. Median age was 60 (range 38–83). Diagnoses included recurrent endometrial cancer of the vaginal cuff in 5, cervical cancer stage IIIB in 4, stage IVA in 1, vaginal recurrence of cervical cancer in 1, and stage II vaginal/urethral cancer in 1. Median tumor size was 5.6 cm (range, 1.1 to 13 cm). Median number of catheters was 16 (range, 11–35). Median EQD2 D90 and D2cc bladder, rectum and sigmoid dose from brachytherapy was 31 Gy (range, 18–64), 23 Gy (range, 10–46 Gy), 17 Gy (range, 6–30 Gy), 9 Gy (range, 0–29 Gy). The target volume was defined as the high-risk CTV (HR-CTV) as previously described ([13], [14]) and was prescribed to the D90 in general over 5 fractions. All patients had template-based interstitial brachytherapy and not an interstitial-ring or ovoid combination where the insertion depth is shorter and deflection is less of a problem. Informed consent was obtained from all subjects. All patients were placed under general anesthesia and intubated. They were then placed in the lithotomy position, on an MRI-compatible platform that elevated their legs [Figure 1A]. In cervical cancer patients with an intact uterus but no visible cervical os, ultrasound was first used outside of the MR room to assist with tandem insertion, but was not used for catheter insertion. For all cases, MRI-compatible plastic obturators (Best Medical, Springfield, VA) and templates were placed and sutured in place.

The same procedures were followed in all cases. Diagnostic 2D T2-weighted Turbo Spin Echo (TSE) MRI scans were performed along the axial, sagittal and coronal planes; covering the entire pelvis, followed by axial phase-navigated segmented Diffusion-weighted echo-planar MRI scans (Siemens Resolve). Thereafter, 12–30 catheters, instrumented with conventional (passively-tracked) stylets were inserted by the attending radiation oncologist through holes in the template, to locations within and surrounding the tumor based on clinical judgement which included the diagnostic MRI imaging performed prior to stylet insertion and the physician's understanding of the clinical examination and the imaging prior to insertion. After each catheter displacement step, a 1.5 minute T2-weighted scan was performed, to visualize the changes in catheter position. The clinician attempted to navigate all the catheters to the best location possible, within a 60–90 minute period, using the passively-tracked MR method, which formed the baseline catheter locations for this study.

Thereafter, up to 4 conventional stylets were serially removed from within the catheter and replaced by MRTR stylets, which were then actively tracked during further manipulation, in order to more accurately reposition the catheters to the ideal location, as determined by the attending radiation oncologist. Adjustment of catheters occurred while the patient remained inside the bore of the magnet with visualization on an MR-compatible monitor outside the MR bore. After positioning was complete, MRTR stylet removal (pull-back) was performed from within a few catheters to gauge the accuracy of catheter trajectory definition.

The positions of the tracked micro-coils on each MRTR stylet were transferred in real-time to a workstation equipped with the 3D slicer visualization interface (www.slicer.org) [15] through an Ethernet network using the OpenIGTLink protocol [16]. The tracked points were processed to provide the instantaneous stylet tip position and the shaft orientation, which were then overlaid on MRI images of the anatomy, and displayed on an MRI-compatible monitor inside the MR room, which was placed ~0.5 m from the interventionalist. The interventionalist stood at the foot of the MRI bore while manipulating the catheters inside the bore [Figure 1A], to monitor the manipulations in real-time, at rates of 6–16 frames-per-second. To account for deformation of the anatomy during catheter manipulation, new MRI images were obtained every 5 minutes, and the catheter tip locations were then overlaid on these revised images. The clinician used these tools to reposition the catheters, seeking to improve dose coverage of the high-risk critical target volume (CTV). To complete the insertion procedure and deliver data for the final RTP, the three-dimensional (3D) spatial trajectories of each of the catheters was acquired by performing a complete removal (“pull-back”) of the MRTR stylet from within the catheter, with instantaneous tracking of the location of the stylet tip during the removal providing the catheter's 3D trajectory [12].

Imaging and tracking parameters

All MR tracking and imaging were performed in a 3T Siemens (Erlangen, Germany) Verio MRI system.

A two-dimensional T2-weighted axial data set, covering the entire anatomical region from the bladder down to the vagina, was acquired using a TSE sequence (TR/TE/ α =3000ms/104ms/120°, 5 mm slice-width; 205×320 matrix, 224×280 mm FOV, ETL=27, 1.5 min/set) as previously described [11]. The acquired images were used in both the passively-tracked

initial phase of the procedure, and thereafter as the background ('roadmap') on which the location of the actively-tracked catheters was displayed.

A modified MRTR sequence was used [17]. An asymmetric refocusing echo was selected to reduce the short- T_2^* arising from the metallic-stylet's susceptibility. Phase-field dithering (PFD) [17, 18] was employed to reduce the effects of B_1 in-homogeneities and inductive RF coupling from multiple neighboring stylets. Although PFD reduced the tracking speed from the fastest possible rate, ~40 frames-per-sec, it provided enhanced tracking Signal-to-Noise-Ratios (SNR), thus generating improved positional information [19]. The clinical MRTR sequence used achieved positional tracking of $0.6 \times 0.6 \times 0.6 \text{ mm}^3$ spatial resolution. Tracking parameters were; $TR/TE/\alpha = 3\text{ms}/1.89\text{ms}/10^\circ$, $FOV = 300 \text{ mm}$, $matrix = 512$, $bandwidth = 150 \text{ kHz}$, and $PFD = 2-3$, $averages = 2-3$, resulting in frame rates ranging from 16 to 6 Hz.

Devices used for MRTR-based navigation

A commercially-available (1% Lanthanated Tungsten) brachytherapy stylet (length 30 cm, diameter 1.6 mm) was modified to render it active. Two 3-layer flexible printed circuit loop coils, which served as the MRTR coils, were placed on the distal end of each stylet [Figure 1B]. The proximal end of the MRTR stylet contained an RF tuning-matching box, which contained tunable inductors, tunable capacitors, as well as crossed (anti-parallel) diodes. The inductors and capacitors were tuned to the 3T field and matched to 50 Ohms, providing optimized tracking SNR. The active stylets used in the study were constructed by MRI Interventions Inc. (Irvine, CA). They were tested for compliance with the requirements of gas re-sterilization and repeated-use mechanical strength, and thereafter used for 3 patient cases each.

A patient isolation box [Figure 1D] was connected to each stylet to ensure patient safety. This box contained a capacitor on each electrical transmission line, to prevent $<10 \mu\text{A}$ direct-current (DC) and $>4 \text{ kV}$ line-current (60 Hz AC) signals, should they propagate on the more proximal electrical lines, from reaching the stylet, as required by IEC/NEMA regulations for MRI-compatible devices [20].

From the patient-isolation box, the signals from the micro-coils were transferred to the MR system via a dedicated eight-channel receiver [Figure 1C]. The receiver possessed a customary Siemens (Erlangen, Germany) coil plug with a corresponding coil file that permitted combination of the MR-tracking coils with multiple imaging coils, such as the Siemens spine coil and body phased-array coil. This capability enables rapid high-resolution imaging to be performed concurrently with MR-tracking. The coil combination also allowed for performing quality-assurance, in order to rapidly determine that the MRTR coils, as well as the entire MRTR acquisition pipeline, were properly functioning, since the signals from the MRTR coils were readily observed as hyper-intense dots on the combined tracking-coil/imaging-coil images.

Data Processing

At the end of catheter insertion, the clinician performed a segmentation of the tumor boundaries and the location of neighboring viable tissues, using the T2-weighted MRI

images, as part of the final RTP. In order to evaluate the importance of catheter-location changes performed during the MRTR phase of the procedure, we utilized this data.

Contours of the segmented tissues were overlaid on the T2-weighted images, using the 3D SlicerRT package. The tracked-catheter paths, over time, were also added to these images, resulting in a temporal map of the catheter manipulation.

The tracking data was analyzed using MATLAB (Natick, MA) software. Four parameters were calculated for every catheter motion using the position of each tracking point, $P_i(x, y, z)$, where the time (t) varied from 0 to T , the end of the sequence of active manipulations; (a) the absolute displacement between consecutive tracking points ($P_t = \|P_{t+1} - P_t\|$), (b) the absolute displacement between the first and last time point ($D = \|P_T - P_0\|$), (c) the total distance of the catheter motion, calculated as the summation of all the displacements

between consecutive tracking points ($S = \sum_0^T \Delta P_t$), and (d) the average speed of motion ($\bar{v} = S/T$).

Results

Patient Safety

No adverse effects were recorded in all 11 patients as a result of the utilization of active MR tracking. Addition of the active tracking segment to the conventional (passively-tracked) catheter insertion procedure, with up to six catheters per patient being actively repositioned, added a total of <15 min to the procedure time.

MRT Tracking performance

We present, from the 11 patient results, 3 scenarios that showcase the accuracy and speed of MRTR in three different modes of motion:

Scenario 1. Catheter trajectory visualization (“pull-back”)—In Figure 2, two stylets were pulled back a distance of 174 mm (green) and 223.7 mm (red), in a time span of 6.03 and 7.99 s, respectively. The motion was recorded at a tracking rate of ~12 Hz, providing 75 and 99 tracking points, with an average distance between tracking points of 2.3 ± 2.1 and 2.3 ± 1.6 mm, respectively.

Scenario 2. Catheter lateral repositioning—In Figure 3, a reposition of an individual stylet is shown. The stylet was first pulled back a distance of 44.8 mm and then reinserted 234.5 mm. The total displacement between the starting point and the last position of the stylet was 43.6 mm. The full reposition was performed in 22.1 s: the extraction took 4.2 s, while the insertion lasted 17.9 s. A total of 139 tracking points were obtained at a tracking rate of ~6 Hz, with an average displacement between tracking points of 2.0 ± 1.3 mm.

Scenario 3. Multiple catheter location adjustments—In Figure 4, four separate catheter repositions were performed. The changes in location for the green, blue, yellow and red stylets were 16.2, 16.3, 16.6 and 26.6 mm, respectively. The motion was tracked at ~16 Hz, for a total of 65, 39, 22 and 56 s, obtaining a total of 400, 241, 137 and 348 tracking

points in each corresponding motion. The mean displacement between tracking points was 2.3 ± 1.9 , 0.8 ± 0.9 , 1.5 ± 1.1 and 1.7 ± 1.8 mm, respectively.

To study the repositioning accuracy, we subdivided the data into two forms of motions: a *coarse repositioning motion*, used while the stylets were extracted and then initially reinserted, and a *fine-tuning repositioning motion*, used when the stylets were moved carefully, to best approach the target, within the time constraints of the procedure. The metrics of these are summarized in Table 1.

After *coarse repositioning* was completed, the stylets were found to be at a mean distance of 11.1 mm from the final position. The speed of this coarse repositioning (an average of 33.4 ± 27 mm/s for all the patients) is approximately equivalent to that possible with ultrasound imaging and electromagnetic-tracking (within a CT scanner) guidance. The ability to see the tumor location continuously during the *fine-tuning repositioning mode* allowed the physician to place the stylet an average of 7 mm closer to the tumor, using careful and accurately-monitored manipulation.

Using the 11 patient procedures, the catheter displacements in the *coarse repositioning mode* ranged from 4.4 to 43.6 mm (median 15.5 mm) and required a time of 14 ± 4.8 s. In the *fine-tuning repositioning mode*, the catheter displacements ranged from 5.3 to 42.7 mm (median 11.6 mm), performed in a time of 24.1 ± 17.3 s. Complete catheter pull-backs were performed over distances ranging from 35 to 172 mm (median 137 mm) at a speed of 51.8 ± 46.4 mm/s, during 4.7 ± 3.1 s. The fastest pull-back required 0.98 s, at an average speed of 101 mm/s, while the slowest pull-back lasted 9.3 s, at an average speed of 16 mm/s.

Discussion

In previous papers [11, 12], the technical feasibility and accuracy of MRTR-based gynecologic-cancer HDR brachytherapy stylet positioning was demonstrated. In this work, the procedure was successfully applied in 11 patients enrolled on a prospective clinical trial. The active tracking procedure was found to be safe, resulted in acceptable final RTP plans, without causing additional complications, and was well tolerated by all patients.

The results show that use of active tracking presents several benefits: the continuous visualization of the target and the tracking data facilitates accurate and time-efficient catheter placement, which was shown to reduce the mean distance to the desired location by 7 mm. Since MRTR allowed tracking catheter motion at a higher frame rate than possible with passive tracking, attempting to obtain such positional improvement with passive tracking would have required a far longer time.

As a result, we believe that future catheter placement procedures can be considerably shortened by using a complete set of actively tracked stylets, without inserting any passively-tracked stylets, since locating the actively tracked catheters is performed at higher speed and with higher spatial accuracy.

Several MRI vendors offer an interactive real-time imaging application, in which sub-second images are acquired, with the acquisition orientation and locations interactively controlled

by the user. In previous studies, we attempted to use this application for stylet guidance, but found that the low inter-tissue contrast and low spatial resolution offered by such images were insufficient to accurately guide the stylets. In addition, a considerable amount of time is required to locate the stylets. In the future, it may be possible to merge this application with MRTR, in order to acquire on-demand images at the tip of the stylet, which may be important for guidance when navigating close to critical structures.

During active-tracking, the physician observed a continuous stream of tracking points, each labeled with a different color, providing a clear identification of the specific stylet being manipulated, which allows the clinician to correct the stylet positions in real time. The active-tracking procedure replaces passive image-based MRI-guided brachytherapy, in which it is impossible to visualize catheter manipulation in real time.

Accurate reconstruction of the full catheter trajectories was also enabled, improving on the resolution and reconstruction speed of RTP obtained from (the currently standard) image-based reconstruction methods. MRTR catheter trajectories, as compared to CT-tracked trajectories, showed mean differences along x, y and z of 0.4, 0.6 and 0.2 mm, respectively, and a total 3D difference of 0.7 mm [21]. These results agree with previous studies [12] and support the possibility of eliminating the currently-required (post-insertion) CT scan from the procedure. This may enable MR-based brachytherapy RTP planning of interstitial implants without ionizing radiation.

MRTR also offers the potential of eliminating the need for a time-consuming manual digitization process of each stylet's trajectory from MR images to obtain the final RTP, which is required when using passive tracking. In contrast, transabdominal ultrasound-guided catheter insertion is feasible but does not allow digitization along the final trajectory.

Additionally, the actively-tracked catheter locations provided continuously during the procedure can be immediately sent to a commercial RTP program and produce an instantaneous RTP dose map. We simulated this process using data acquired from one of these cases, and demonstrated that such an adaptive RTP can be used for intra-procedural dosimetric evaluation. Adaptive intra-procedural RTP can provide a means for quantifying the dosimetric advantages of (i) continued catheter manipulation of the catheters already inserted, as well as (ii) inserting additional catheters. The advantages may be to allow higher and/or more uniform dose to tumor regions, while sparing neighboring tissues.

In conclusion, MR-tracking during gynecologic interstitial brachytherapy insertion is feasible and permits rapid targeting and catheter digitization.

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Figure 1. MRTR-guided HDR gynecologic-cancer brachytherapy setup

(A) Physician placing the stylets inside the MRI during the procedure. (B) Actively tracked stylet. Inset: Active tracking micro-coils in the stylet's tip. (C) Dedicated 8-channel MRI preamplifier unit. (D) Patient isolation unit, placed between the MRTR stylet and the MRI preamplifier unit, which prevents electrical currents, if they propagate on the electrical lines, from reaching the patient's body.

Figure 2.

Axial (A), sagittal (B) and coronal (C) MRI images from a case where two catheters were pulled back with real-time MR monitoring during the catheter adjustment. The images are overlaid with clinician-segmented areas of CTV (Orange), sigmoid (Blue), bladder (Yellow), vagina (Pink) and rectum (Brown). The location of each MRTR-tracked catheter over time, during manipulation by the clinician, was superimposed using green and red dots. Cross and star signs mark the starting and ending points of the motion, respectively. Continuous trajectories of the green and red catheters are displayed in panels D and E, respectively.

Figure 3.

Axial (A), sagittal (B) and coronal (C) MRI images from a case where a catheter was pulled-back and then re-inserted, obtaining an improved location. The images are overlaid with clinician-segmented areas of CTV (Orange), bladder (Yellow), vagina (Pink) and rectum (Brown). The location of each MRTR-tracked catheter over time, during manipulation by the clinician, was superimposed using red dots. Cross and star signs mark the starting and ending points of the motion, respectively. A continuous trajectory of the catheter is displayed in panel D.

Figure 4.

Axial (A, D), sagittal (B, E) and coronal (C, F) MRI images from a case where four catheters were repositioned. The images are overlaid with clinician-segmented areas of CTV (Orange), bladder (Yellow), vagina (Pink) and rectum (Brown). The tracking data is displayed on duplicate MRI images to facilitate easier visualization. Each tracked catheter was superimposed using yellow, red, green and blue dots. Cross and star signs mark the starting and ending point of the motion, respectively. Continuous trajectories of the green,

blue, yellow and red catheters are displayed in panels G, H, I and J, respectively. Although motion was smooth, some trajectories may appear jagged due to noise.

Statistics from the same case shown in Figure 4. Each catheter motion has been subdivided into *coarse* (c) and *fine-tuning* (f) *repositions*. *Coarse repositions* consisted of pull-backs and push-forward motions, typically performed at a faster rate and with larger average distance between tracking points. *Fine-tuning repositions* were performed at a slower pace, attempting to bring the catheter closer to the clinician's desired location. Slower motion provided higher accuracy placement, with smaller average distances between successive tracking points.

Table 1

Motion	Total displacement (mm)	Distance between starting and final point (mm)	Time (s)	Tracking points	Average distance between points (mm)
Green (c)	152.9	4.4	8.94	55	2.8 ± 1.8
Green (f)	523.6	11.3	40.00	249	2.1 ± 1.8
Green (c)	242.0	9.6	15.53	98	2.5 ± 2.0
Blue (c)	193.9	15.5	6.09	39	5.0 ± 3.1
Blue (f)	146.1	8.3	8.49	54	2.7 ± 1.6
Blue (c)	267.6	16.9	12.49	79	3.4 ± 2.6
Yellow (c)	392.0	14.2	16.50	104	3.8 ± 7.1
Yellow (f)	53.6	2.3	5.28	34	1.6 ± 1.3
Red (c)	197.1	16.3	13.42	83	2.4 ± 1.8
Red (f)	395.3	6.1	42.73	266	1.5 ± 1.8