

RADIOTHERAPY QUALITY ASSURANCE OF GYNECOLOGIC ONCOLOGY GROUP (GOG) PROTOCOL 165, A COOPERATIVE GROUP STUDY OF CARCINOMA OF THE CERVIX

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ABSTRACT:

GOG protocol 165 was a randomized phase III trial to evaluate radiation vs. radiation plus weekly cisplatin vs. radiation plus protracted venous infusion 5-FU in patients with stage II-B, III-B and IV-A carcinoma of the cervix. Protocol treatment included external beam therapy and high-dose rate or low-dose rate brachytherapy. Historically, GOG has performed an extensive review of patient treatments on their clinical trials. As HDR had not previously been used in GOG trials, credentialing of institutions and physicians was required prior to entering patients onto the study for the use of HDR, but was not required for external radiation therapy or LDR.

Credentialing consisted of a review of the institution's HDR physics and QA, and a clinical and dosimetric review of the brachytherapy treatment of two patients treated by the same radiation oncologist in a manner similar to the protocol guidelines. The credentialing process not only evaluated the quality of HDR procedures at the institution, but also assured that the institution and participating radiation oncologist had HDR experience. At the same time, it educated the institution as to the specific requirements of the protocol.

Retrospective review of radiotherapy of 326 patients entered on the study was performed. A recalculation of patient dose and a review of the records and all planning and verification films were performed by the Radiological Physics Center in conjunction with the GOG HDR subcommittee and the protocol study co-chairs, respectively.

Deviations from protocol guidelines were assessed according to predefined criteria. 100% of the patients treated at credentialed institutions were treated without major protocol deviations. In contrast, 81% of patients from non-credentialed institutions completed treatment without major deviations. Minor deviations occurred in both groups with the result that 75% and 50% of patients from credentialed and non-credentialed institutions respectively were treated in strict compliance with the protocol. A breakdown of protocol deviations appears in table 1.

Table 1. Summation of Deviations for Non-Certified and Certified Institutions

Types of Deviations	Dose	Elapsed Time	External Beam Field Placement	Brachytherapy	External Boost
Major for non-certified Inst.	24% (16 patients)	28% (18 patients)	28% (19 patients)	18% (9 patients)	
Minor for non-certified Inst.	4% (13 patients)	5% (14 patients)	22% (58 patients)		1% (2 patients)
Minor for certified Inst.		3% (2 HDR Patients)	20% (10 HDR Patients & 3 LDR Patients)		2% (1 LDR Patient)

QA is an important component of clinical trials. The frequency of deviations was reduced for those institutions that were credentialed. It seems that those institutions that participated in the credentialing process were better prepared to comply with both the external beam and brachytherapy requirements of the protocol. This may be because through the credentialing process they had received feedback on how to better comply with the treatment protocol prior to submitting a patient onto the study. A dynamic credentialing process of only one aspect of the radiation treatment resulted in greater compliance with the entire radiotherapy treatment. This credentialing process should be used as a model for all protocol groups in future studies in order to enhance the QA of radiotherapy within protocols.

This work was supported by PHS grants CA10953, CA27469 and CA37517 awarded by NCI, DHHS.

INTRODUCTION:

GOG protocol 165 was a randomized phase III trial to evaluate radiation vs. radiation plus weekly cisplatin vs. radiation plus protracted venous infusion 5-FU in patients with stage II-B, III-B and IV-A carcinoma of the cervix. Protocol treatment included external beam therapy and high-dose rate (HDR) or low-dose rate (LDR) brachytherapy. Historically, GOG has performed an extensive review of patient treatments on their clinical trials. As HDR had not previously been used in GOG trials, credentialing of institutions and physicians was required prior to entering patients onto the study for the use of HDR. Credentialing was not required for external beam radiation therapy or LDR.

METHODS:

Credentialing requirements included completion of a questionnaire, a review of the institution's HDR physics and QA, and a clinical and dosimetric review of the brachytherapy treatment of two patients treated by the participating radiation oncologist in a manner similar to the protocol guidelines. The credentialing process not only evaluated the quality of HDR procedures at the institution, but also assured that the institution and participating radiation oncologist had HDR experience. At the same time, it educated the institution as to the specific requirements of the protocol.

Retrospective review of radiotherapy of 337 patients entered on the study was performed. A recalculation of patient dose and a review of the records and all planning and verification films were performed by the Radiological Physics Center in conjunction with the GOG HDR subcommittee and the protocol study co-chairs, respectively.

RESULTS:

Deviations from protocol guidelines were assessed according to predefined criteria. 100% of the patients treated at credentialed institutions were treated without major protocol deviations. In contrast, 76% of patients from non-credentialed institutions completed treatment without major deviations. Minor deviations occurred in both groups with the result that 73% and 45% of patients from credentialed and non-credentialed institutions respectively were treated in strict compliance with the protocol.

SUMMARY:

QA is an important component of clinical trials. The frequency of protocol deviations was reduced for those institutions that were credentialed. It seems that those institutions that participated in the credentialing process were better prepared to comply with both the external beam and brachytherapy requirements of the protocol. This may have been because the credentialing process provided feedback on how better to comply with the treatment protocol prior to submitting a patient onto the study. A dynamic credentialing process of only one aspect of the radiation treatment resulted in greater compliance with the entire radiotherapy treatment. This credentialing process should be used as a model for all protocol groups in future studies to enhance the QA of radiotherapy within protocols.

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Total Percent Deviations for Credentialed and Non-Credentialed Institutions (337 patients)

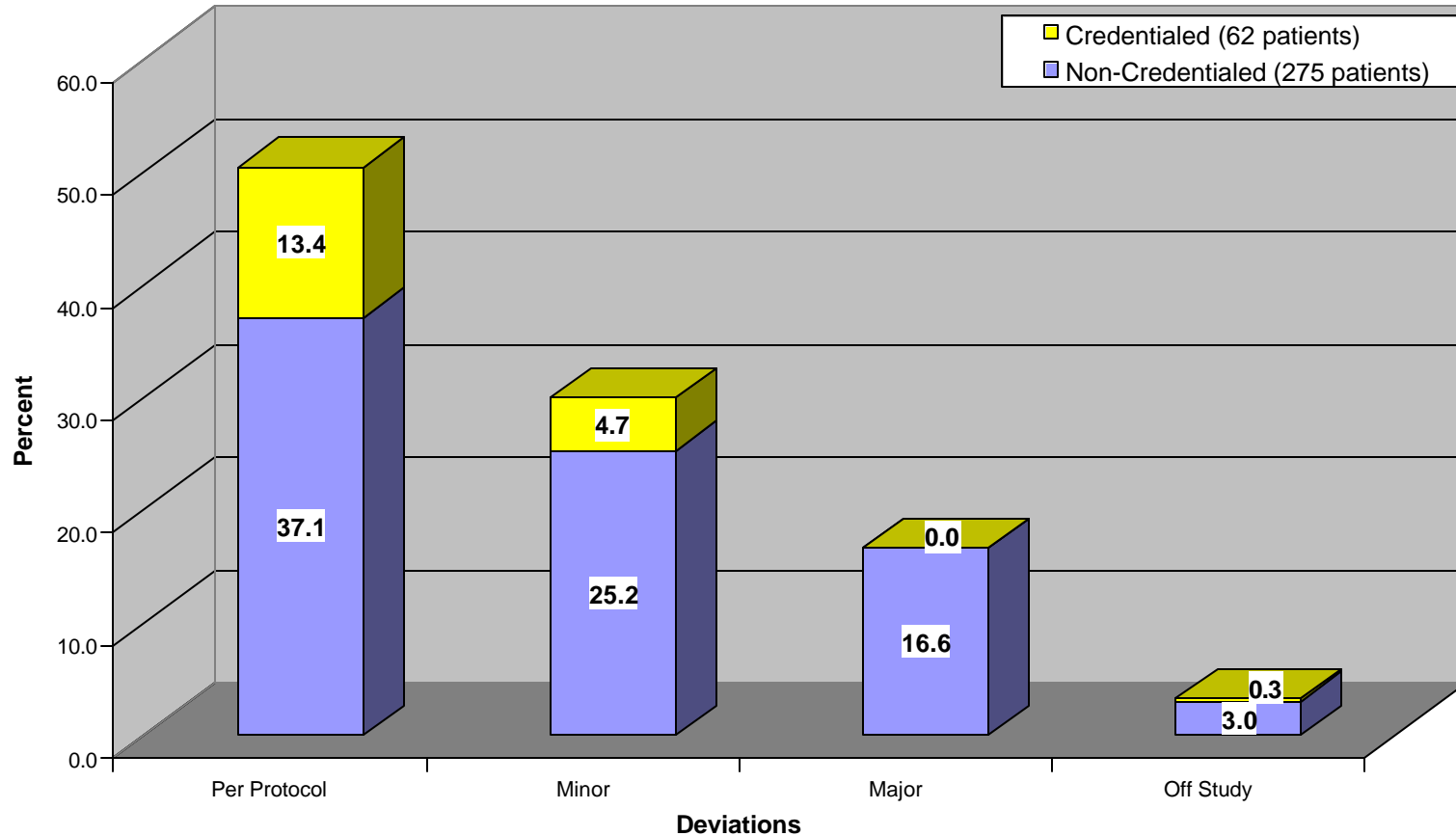


Figure 1: Of those patients that were treated on GOG protocol 165, 50% were treated per protocol, whether or not the institution was credentialed for HDR. Minor deviations were due to field placement, time, dose and/or boost. Major deviations were due to field placement, time, dose or brachytherapy procedure. Institutions that were credentialed to treat with HDR did not commit any major deviations. Those patients classified as off study were due to either patient ineligibility, incomplete RT and/or disease progression.

Major Deviations for LDR Patients from Non-Credentialed Institutions (56 of 275 patients (20%))

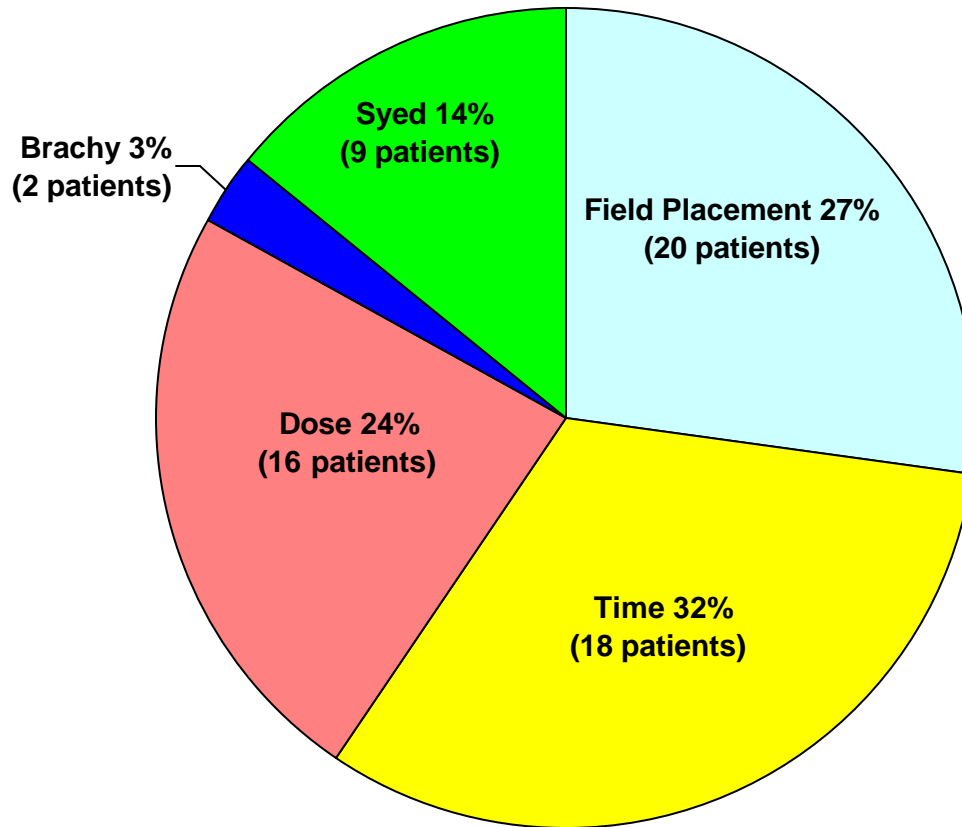


Figure 2: 32% of patients were classified a major deviation because the overall treatment time was too long. 24% of the patients were a major deviation due to dose errors. Of these, one-third of the patients received too high a dose and two-thirds received too low a dose. Major deviations due to field placement (27%) resulted from unacceptable shielding of the critical structures, or incorrect field shape or placement. Syed implants were not to be utilized as a treatment modality on this protocol and their use resulted in 14% of the major deviations. One patient was classified a major deviation because the institution used HDR without first obtaining credentialing. Another patient's intracavitary implant geometry was unacceptable.

Institutions Credentialed for HDR (23 patients treated with LDR and 39 patients treated with HDR)

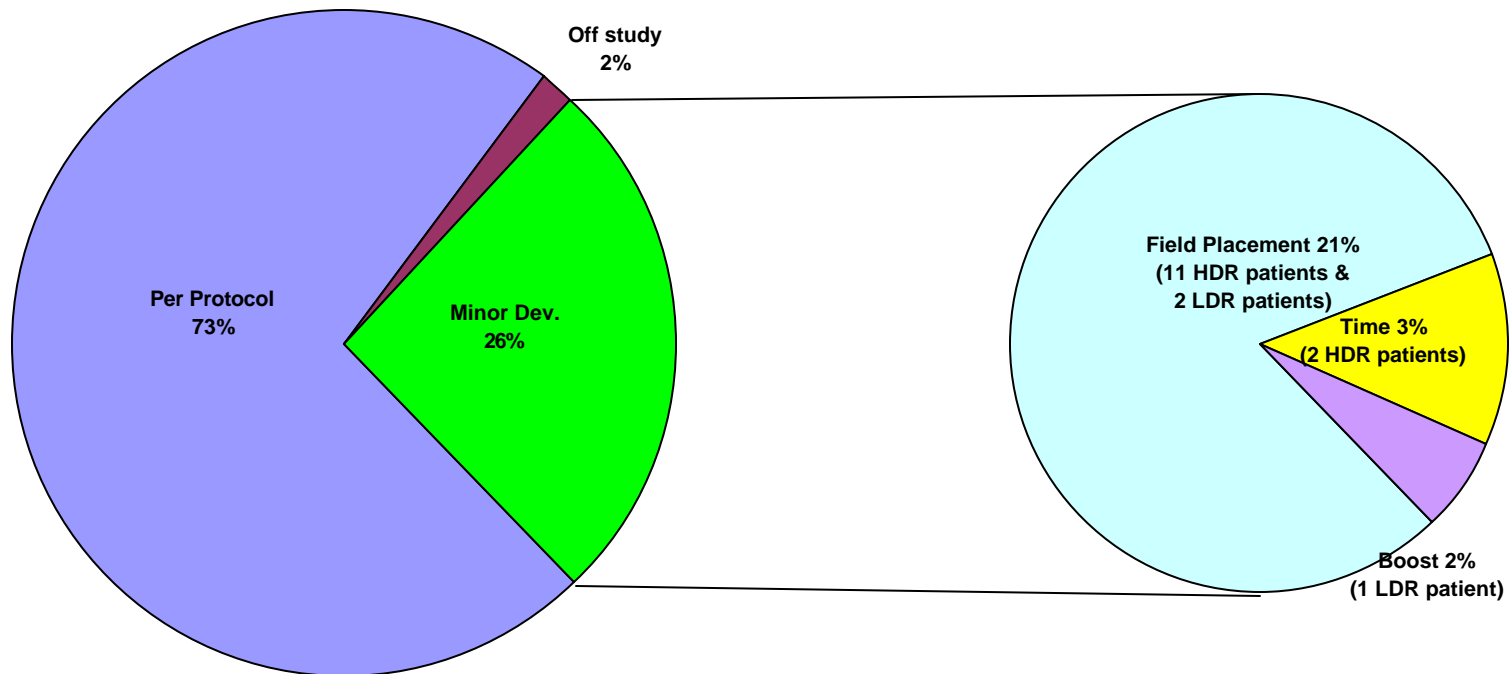


Figure 3 & 4: Both credentialed and non-credentialed institutions received minor deviations due to field placement, time and dose. Minor deviations in field placement were due to unacceptable shielding of critical structures, or incorrect field shape or placement. Institutions also received deviations if the overall treatment time was too long. Two-thirds of the patients treated at non-credentialed institutions were judged minor deviations because the dose was too low.

**Total Deviations for Non-Credentialed Institutions
(275 patients, all LDR)**

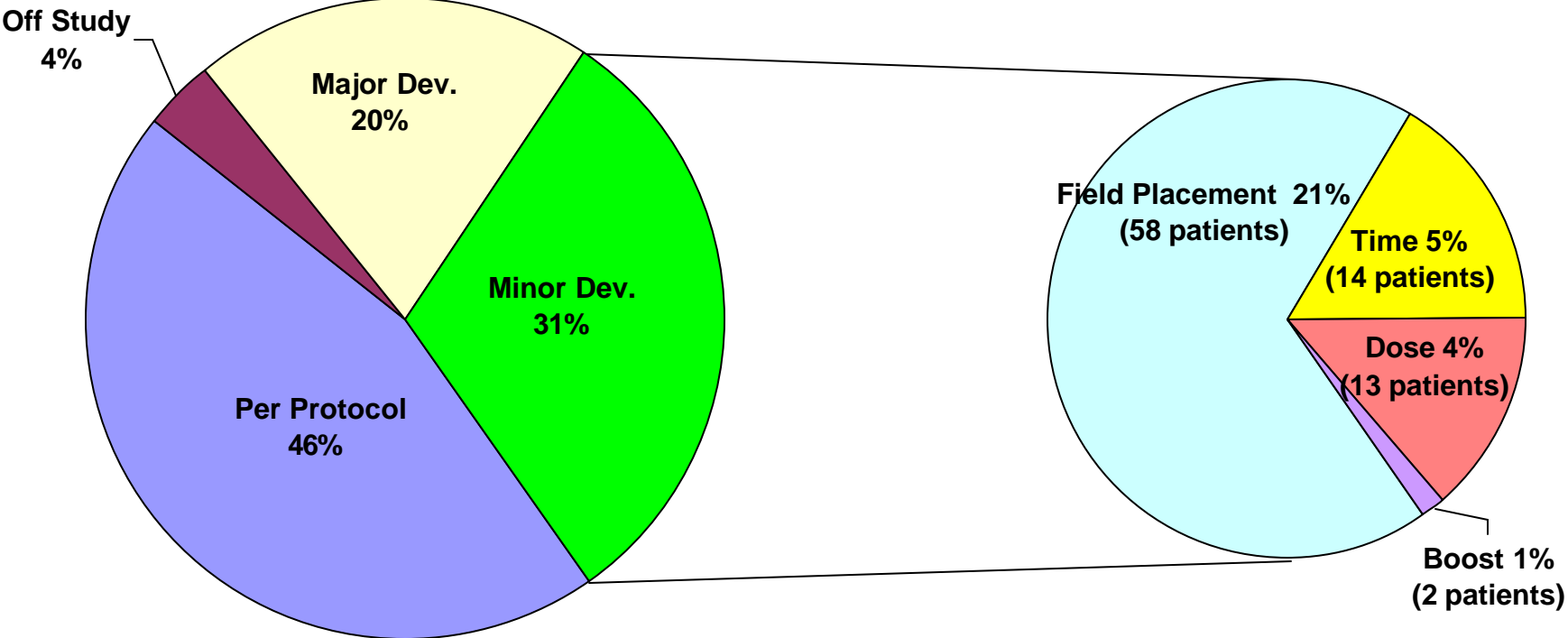


TABLE 2 : GOG QUALITY CONTROL GUIDELINES FOR EVALUATION OF RADIATION THERAPY FACTORS

	Prescribed Dose	Prescribed Daily Fractionation	Elapsed Time (Days)	Port Volume
Fully Acceptable	≤ 5% ≤15% (Brachy)	≤ 5%	≤ 10%	Tumor treatment volume included in field
Minor Deviation	6% - 10% 16% - 25% (Brachy)	6% - 10%	11% - 20%	*
Major Deviation	11% - 20% >25% (Brachy)	11% - 20%	> 20%	*
Unacceptable	> 20%	> 20%	Over 4 week interruptions (except for split course)	Tumor treatment volume not satisfactorily included in treatment volume

* If field margins are tight or critical structures are questionably shielded the treatments are classified a minor or major deviation based on volume.

HDR Brachytherapy Credentialing Application

Administration:

I. Institution Performing HDR:

Institution Name: _____

Institution Study Group #: _____

Address: _____

II. HDR Personnel:

A. Radiation Oncologist(s) performing implants

Voice Number

Fax Number

() - () -

() - () -

() - () -

B. Physicist(s) Responsible for HDR

Voice Number

Fax Number

() - () -

() - () -

() - () -

C. Dosimetrist(s) responsible for Treatment Planning

Voice Number

Fax Number

() - () -

() - () -

() - () -

C. Clinical Research Assoc./ Data Manager

Voice Number

Fax Number

() - () -

Therapy Unit:

I. HDR Unit:

Manufacturer and Model: _____

Source Supplier: _____

Frequency of HDR Source

Replacement: _____

Dosimetry Quality Assurance:

II. Quality Assurance (please attach the following):

- A. Source strength verification:
Submit a description of the procedures followed to verify the calibration of the source(s).
Include:
- Description of dosimetry system.
 - Confirmation that calibration meets national standards.
 - Measurement and calculation techniques, including conversion of the above standard into the source specification units, used by your treatment planning computer.
 - Frequency of calibration.
 - Source certificate.
- B. Source positioning in the catheter:
- Describe quality assurance (QA) procedures used to verify that source positions within the catheters are known and reproducible.
- C. Dosimetry procedures:
- Describe the exact procedure followed to assure that the dose calculations are in accordance with the requirements of the protocol.
- D. Other quality assurance procedures:
- Describe any hand calculations done to verify the accuracy of the computer-generated treatment plan.
 - Submit the sample monthly and daily QA checks (if not included in the data submitted for the non-protocol patient in section IX.)
 - Describe any other QA procedures pertinent to study objectives.

III. Treatment Planning Computer:

Manufacturer and Model: _____

Software/Version: _____

Clinical:

I. Make and Model of GYN Applicators _____

II. Implant films:

- Localization Technique:

Where are Films Taken:

Simulator (Orthogonal Pair)

In HDR Room

Conventional x-ray (Orthogonal Pair)

where: _____

Other: _____

- Geometry of dummy sources. (How do you determine where the end of the catheter will be and where the 1st seed location will be? Attach diagram(s) if helpful.)

Clinical (Cont'd):

III. Implant films (cont'd):

- How do you identify cervical os?

- Patient Positioning:

Lithotomy Position

Supine with pillow support under

Supine, flat

Other: _____

- Is patient position changed between filming and treatment?

Yes

No, explain: _____

Description of the procedure (completed by the radiation oncologist-similar to op notes) including discussion of the procedure to assure comparable implants every time:

Benchmark Cases:

I. Please include the following (please attach):

- A. Dose distribution about the source in two planes (equator and polar)
- B. Complete radiation therapy data on two non-protocol patients, per physician, treated to this protocol, including:
 - films of all insertions
 - dose distribution on all insertions
 - summation of dwell times and positions
 - procedure notes for all insertions
 - treatment printouts for all insertions
- C. mail all the materials (including this application) to:

HDR Brachytherapy Credentialing
C/O Jessica Lowenstein
Radiological Physics Center
7515 S. Main Street, Suite 300
Houston, TX 77030

Many applications we receive are incomplete, therefore we recommend that you call prior to submitting your application and we will verify that the data is complete. You can contact us at (713) 745-8989, ask for either Joye Roll or Jessica Lowenstein.