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Tafaul-Al-Ahsa Cancer Foundation Wins EXCELLENCE AWARD for Cancer Awareness Initiatives at Gulf Cancer Awareness Week 2024





The Gulf Oncology Society meeting resulted in fruitful outcomes, with young doctors showing keen enthusiasm for assuming leadership roles and implementing impactful initiatives.

The Official Journal of the Gulf Federation For Cancer Control

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Original Article

Clinical Outcomes and Dosimetric Evaluationof Interstitial Brachytherapyin Gynecological Malignancies

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Abstract

Background : In management of Carcinoma Cervix, Brachytherapy plays a crucial role. Most commonly used technique is Intracavitary Brachytherapy (ICBT). In cases where ICBT is not technically feasible or it may result in suboptimal dose distribution, Interstitial Brachytherapy (ISBT) is recommended. With this study we wanted to study the clinical outcome and dosimetric details of interstitial brachytherapy in gynecological cancers.

Materials & Methods: We analysed clinicaloutcome and dosimetric details of interstitial brachytherapy (ISBT) done for gynecological malignancies in our institute during the period 1st January 2013 to 31st December 2020.

Results: Total of 42 interstitial brachytherapy (ISBT) details were analysed.37 patients had Carcinoma Cervix and 5 patients had Carcinoma Vagina. In the majority of the patients, ISBT dosage schedule was three fractions 7Gy each. D2cc to rectum, bladder, sigmoid and bowel were 4.88 Gy, 5.62 Gy, 3.57 Gy and 2.47 Gy respectively. Mean CTV volume was 129.89 cc. EQD2 dose to CTV combining EBRT and ISBT dose was 85.88 Gy. D90 and D100 to CTV from ISBT were 111.96% and 68.21 % of prescribed dose respectively. Grade III/IV toxicities were seen in 5 (12%) patients. Local control rates at 1year & 2 years were 88% & 85.7% respectively. DFS at 1 year, 2 years and 3 years were 80.7%, 72.3% and 65.7% respectively. OS at 1year, 2 years, 4 years and 5 years were 92.5%, 65.5%, 59.5% and 42.3% respectively.

Conclusion: 3D imagebased dosimetry with CT based planning using MUPIT implant is a feasible option for gynecological malignancies warranting interstitial brachytherapy. In view of good clinical outcomes in terms of toxicity profile, Local control, DFS and OS with acceptable GEC–ESTRO dosimetric data, we recommend routine use interstitial brachytherapy if facilities are available and in clinical situations were ISBT is indicated.

Keywords : Interstitial Brachytherapy, Gynecologicalmali gnancy,Carcinoma Cervix

Introduction

Worldwide annual incidence of Carcinoma Cervix is around 570,000. Carcinoma Cervix is one among the leading cause for cancer death in women worldwide. Global annual incidence of Carcinoma Vagina is around 18,000.[(1)]Intracavitary Brachytherapy (ICBT) has improved clinical outcome in Carcinoma Cervix.[(2–4)] Most common site treated with Brachytherapy is Carcinoma Cervix as per the survey done by American Brachytherapy Society (ABS).[(5)] In management of Carcinoma Cervix Brachytherapy plays a crucial role. Intracavitary Brachytherapy (ICBT) is the most commonly used technique. In cases where ICBT is not technically feasible or it may result in suboptimal dose distribution, Interstitial Brachytherapy (ISBT) is recommended.[(5,6)] The most common technique for ISBT is perineal template based implant procedure.

In Radiation treatment of vaginal tumors both primary and recurrent cases, Brachytherapy plays a crucial role. After external beam radiation to pelvis, a brachytherapy boost is used to treat vaginal cancers. Primary and recurrent cancers in the vagina are often treated with a brachytherapy boost after external beam radiation to the pelvis. Brachytherapy delivers high–dose radiation to tumors due to the ability to place the source in close proximity or inside the target. Commonly used Brachytherapy techniques in vaginal tumors are single–channel vaginal cylinder (SCVC) and ISBT. ISBT

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is the preferred modality for vaginal cancer lesions thicker than 5 mm as per recommendations of American Brachytherapy Society.[7] Various interstitial templates like Martinez Universal Perineallnerstitial Template (MUPIT) and Syed Neblett template are used in clinical practice for gynecological malignancies.[8,9] With this study we intented to assess the clinical outcome and dosimetric details of Interstitial Brachytherapy for gynecological malignancies done in our institution.

Patients and Methods

This was a retrospective study done in a tertiary cancer centre. All patients who underwent ISBT during the period January 1st 2013 to December 31st 2020 were included in the study.

Interstitial Brachytherapy Procedure

Clinical and imaging findings prior to EBRT and brachytherapy were used to estimate tumor volume and number of needles required for implantation. Under general anesthesia / Epidural anesthesia pelvic examination was performed to evaluate extent of residual disease. Bladder was catheterized with Foleys catheter and the balloon was filled with 7 cc dilute omnipaque. Under transabdominal Ultrasound guidance, a tandem was placed in the uterus and a vaginal obturator was placed in the vagina. Following which four corners of the templatewas sutured to the perineal region for proper immobilization. After that the needles were carefully inserted through the template under Ultrasound guidance. After the procedure patient was shifted to CT simulator and planning CT was taken after administering contrast into bladder.1mm slice thickness planning CT scan was taken. The CT images were imported to Oncentra Treatment Planning System and the Radiation Oncologist meticulously contoured clinical Target Volume (CTV) and organ at risk (OAR). Appropriate dose was prescribed to CTV and planning was done by Medical physicist. Figure 1 shows interstitial done for a patient. Figure 2 shows axial CT image with interstitial implant, CTV and OARs. Figure 3 shows sagittal CT image with interstitial implant, CTV and OARs Once the plan was generated the plan was approved after carefully noting the CTV coverage and OAR doses from the dose volume histogram (DVH). Various 3D DVH parameters including 0.1cc,1cc,2cc doses to the OARs were noted CTV volume, D90 and D100 to CTV also were noted. Once the plan was approved, the same was sent to Nucleotron 20 channel HDR Brachytherapy machine and treatment was delivered. The subsequent fraction of HDR Brachytherapy was delivered after a minimum gap of 6 hours.

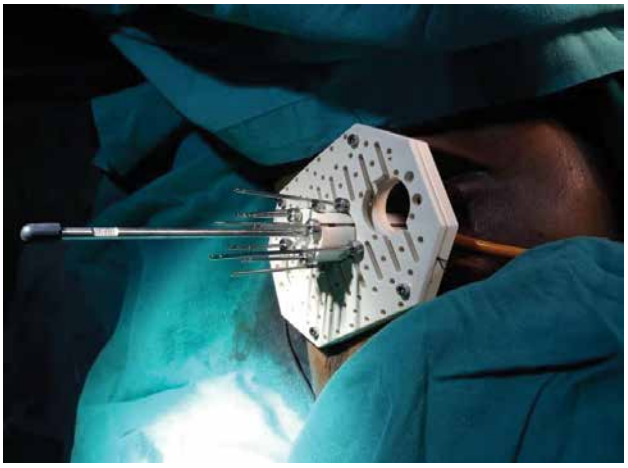


Figure 1 shows the image of an Interstitial implant.

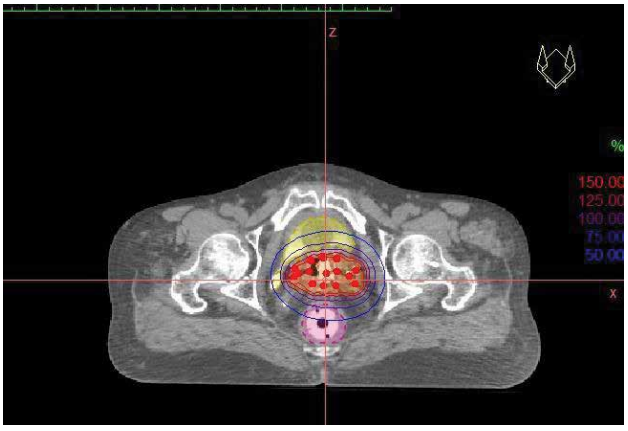


Figure 2 shows axial CT image with interstitial implant, CTV & OARs

CTV in red, Bladder in yellow, Rectum in pink

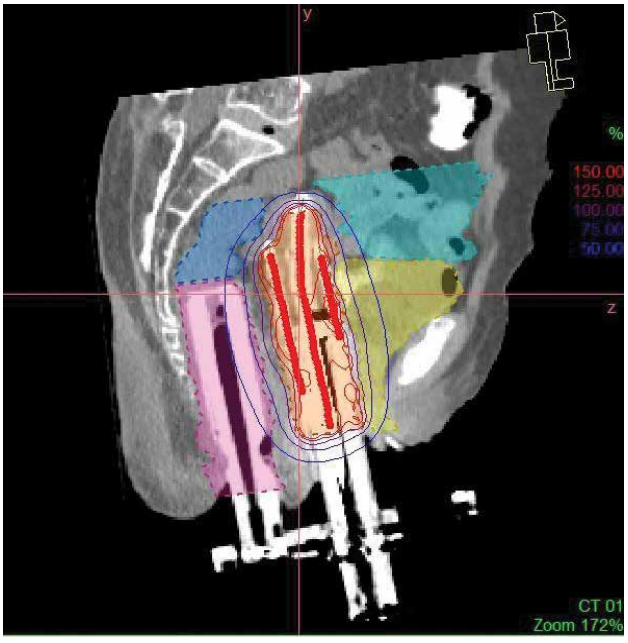


Figure 3 shows Sagittal CT image with interstitial implant,CTV& OARs

CTV in red, Bladder in yellow, Rectum in pink, Sigmoid in dark blue & Small bowel in light blue.

Analysis of brachytherapy plans from oncentra treatment planning system was done. Demographic data of patients who underwent ISBT for gynecological malignancies in our institution during the period from 1st Jan 2013 to 31ST December 2020 were collected from case sheet. GEC–ESTRO DVH parameters for the doses delivered to 90% and 100% of the CTV ie. D90, D100 were recorded. OAR (rectum , bladder , sigmoid and small bowel) doses were also noted from the DVH . Clinical outcome like local control of disease, disease recurrence (local,regional,distant) andtoxicities were documented from case records after reviewing the follow up details carefully.

Statistics

Descriptive statistics like Frequencies, Percentages, Median, Mean with standard deviation were used wherever appropriate. DFS & OS were determined using Kaplan Mier method.

Results

Total of 42 patient details, who underwent Interstitial Brachytherapy (ISBT) were analysed. Demographic details of the patient who underwent ISBT are shown in Table 1.

Variable	No.of patients
Age	Median : 55 years (Range : 41–69)
Primary tumor site Carcinoma Cervix Carcinoma Vagina	 37 (88%) 5 (12%)
Histology Squamous cell carcinoma Adenocarcinoma	 39(93%) 3(7%)
FIGO Stage Carcinoma Cervix III A III B III C1 III C2 IV A Carcinoma Vagina II III	 5 (12%) 16 (58%) 11(26%) 4(10%) 1(2%) 1 (2%) 4 (10%)

Table 1 shows Demograhic details of patients who underwent ISBT

Out of the total 42 patients, 37 patients had ISBT alone and rest for patients had both ISBT and ICBT. External Beam Radiotherapy given was not uniform for all patients. 16 each patients received fractionation schedule of 50.4 Gy in 28 fractions and 55 Gy in 25 fractions. Other fractionation schedules were 50Gy in 25 # in 4 patients, 45 Gy in 25 # in 2 patients, 46 Gy in 23 # in 3 patients and 54 Gy in 27 fractions. In majority of patients, 30 out of 42, Interstitial Brachytherapy (ISBT) schedule was three fractions 7 Gy each. 3 fractions of 5 Gy each was given in 5 patients, 4 fractions 6 Gy each was given in 3 patients, 4 fractions each 6.5 Gy in 2 patients, 4 fractions 5.7 Gy each in 1 patient and 3 fractions 6.35 Gy each in 1 patient.

Mean CTV volume was 129.89 ± 47.25 cc and ranged from 22 to 235 cc.Since interstitial Brachytherapy fractionation schedule was not same for all patients D90 & D100 are mentioned as percentage of prescribed dose. D100 CTV was 68.21 % and D90 CTV was 111.96%. GEC ESTRO Organ at risk (OAR) dose to D2cc to Rectum, Bladder, Sigmoid and Small bowel & EQD2 doses to OARs are shown in Table 2.

Organ At Risk (OAR)	D2cc in Gy (Mean ± Standard Deviation)	EQD2 doses (Mean ± Standard Deviation)
Rectum	4.88 ± 0.93	74.1 ± 6.45
Bladder	5.62 ± 0.82	79.90 ± 6.27
Sigmoid	3.57 ± 1.16	63.45 ± 8.55
Small Bowel	2.47 ± 0.89	57.07 ± 4.95

Table 2 shows GEC–ESTRO OAR doses & EQD2 doses to OAR

Mean EQD2 dose to CTV combining EBRT dose and D90 dose was 85.88 ± 16.01 Gy. BED to CTV combining EBRT and brachytherapy dose, assuming an α/β of 10 was 97.8 ± 13.11 Gy.

Late toxicities were seen in 15 (36%) of patients. Most common toxicity being Grade II rectal toxicity in 8 patients. Grade IV rectal toxicity were seen in 4 patients, One patient had Grade IV bladder toxicity and rectal toxicity, one had Grade I bladder toxicity and one had Grade I rectal toxicity.

Local control rate at one year was 88% and at 2 years was 85.7%. 5 patients had residual disease after treatment. Hence the details of 37 patients were used for disease free survival (DFS) analysis. Figure 4 shows DFS analysis. DFS is shown in months. DFS at 1year, 2 years and 3 years were 80.7%, 72.3% and 65.7% respectively. 13 out of 37 patients had disease recurrence on follow up. Most of the patients 10 (77%) had distant metastasis as recurrence.

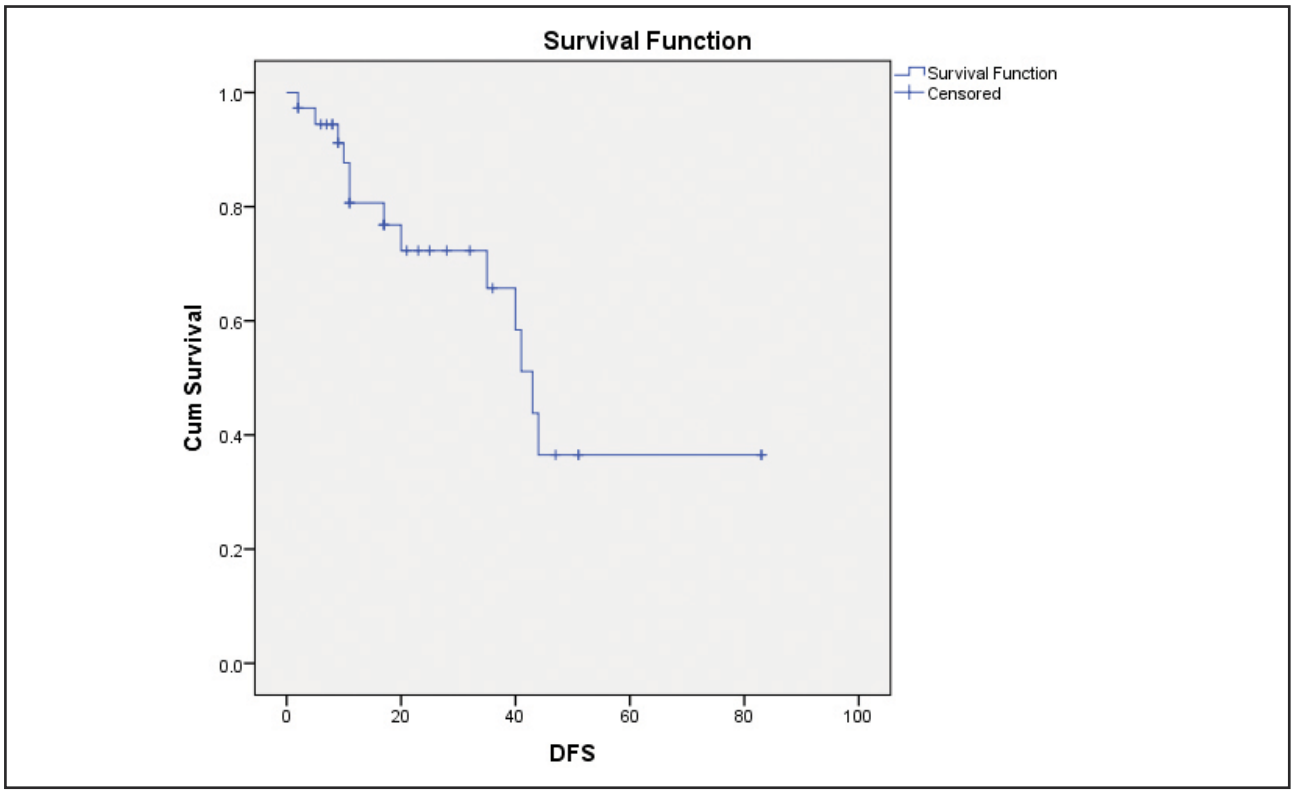


Figure 4 shows Disease free survival (DFS)

Overall survival (OS) of the patients are shown in Figure 5. OS is shown in months. OS at 1year, 2 years, 4 years and 5 years were 92.5%, 65.5%, 59.5% and 42.3% respectively.

Discussion

Median age of patients who underwent ISBT was 55 years and it was similar to studies.[10,11] Around 58% of the patients in our study had Ca Cervix FIGO stage IIIB disease, similar to

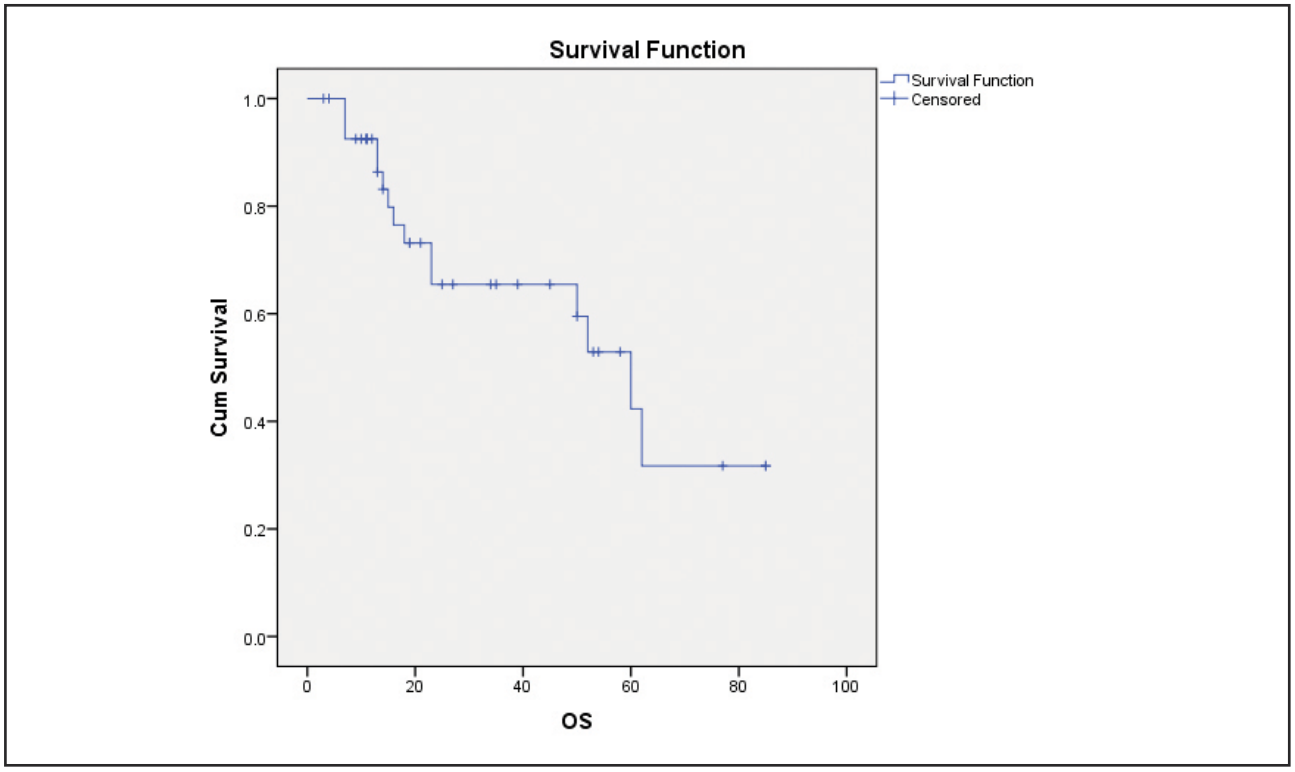


Figure 5 shows Overall survival (OS)

study by Murakami et al. In this study 93% of patients had Squamous cell Carcinoma as in similar studies.[11,12]

In majority of patients (%88) 37, who underwent ISBT had Carcinoma Cervix and rest (%12) 5 of the patients had Carcinoma Vagina. Out of the 42 patients, (%88) 37 patients had ISBT alone and (%12) 5 patients had ISBT and ICBT.Mean CTV was 129.89 cc in our study and it was different from similar studies.[10,11] In our study mean EQD2 dose combining EBRT and D90 of Brachytherapy for CTV was 85.88 Gy and this was slightly higher than in study by Mahantshetty et al and Sharma et al.[12,13] Since ISBT dose was not uniform in all patients, D90 and D100 was assessed as percentage of the prescribed Brachytherapy dose. Mean D90 and D100 were 111.96% and 68.21% respectively. Mean D90 was around 113% of prescribed dose in study by Onoe et al.[10]

Our study showed a mean D2cc to Rectum, Bladder, Sigmoid and Small bowel were 4.88 Gy, 5.62 Gy, 3.57 Gy and 2.47 Gy respectively and it was in accordance with similar studies.[10,14,15]EQD2 doses to OARs like Rectum, Bladder, Sigmoid and Small bowel combining EBRT and D2cc Brachytherapy doses were 74.10 Gy, 79.90 Gy, 63.45 Gy and 57.07 Gy respectively and it was slightly lesser compared to study by Sharma et al.[13]As per ABS guidelines OAR dose constraints for rectum and bladder are 75 Gy and 90 Gy respectively.[7] Our study have reported acceptable dose to rectum and bladder combining EBRT and ISBT. Mean EQD2 dose to CTV combining EBRT and D90 doses was 85.88 Gy and this is considered to be clinically effective dose for adequate tumor control.

Overall late toxicities were seen in (%36) 15 patients. Out of this Grade III/ IV toxicities were seen in (%12) 5 patients. Out of 5 patients who had Grade IV toxicities, 4 patients had recurrent disease after previous Definitive radiation therapy and we had considered for reirradiation. Hence this Grade IV toxicities were expected and explained in advance to these patients. Grade III/ IV rectal toxicity in our study was seen in 5 (12%), which was similar to Mahantshetty et al and in our study one patient had combined Grade IV rectal and bladder toxicity. Grade III/ IV late toxicity was similar to ours in another reported study.[12,16]

Out of the 42 patients, (%12) 5 had residual or persistent disease after treatment. Study by Beriwal et al showed around 18% persistent disease rate in their study.[7] Local control rate at 1 year was 88% and at 2 years was 85.7% respectively and was in accordance with study by Lee et al.[16] DFS at 1 year, 2 years and 3 years were 80.7%, 72.3% and 65.7% respectively in our study and this was slightly better compared to available literature.[12,16] OS reported in our study at 1year, 2 years, 4 years and 5 years were 92.5%, 65.5%, 59.5% and 42.3% respectively. Retrospective nature of the study and small sample size are the limitations of our study.

Conclusion

CT based planning using MUPIT implant is a feasible option for gynecological malignancies warranting interstitial brachytherapy. GECESTRO recommended OAR and CTV parameters helps in plan evaluation and documentation. Our study have shown adequate doses with ISBT to the target region, limiting the doses to OARs to an acceptable level. This study showed good local control rates. Late toxicities were lesser in number and Grade III/IV toxicities were more seen in reirradiation patients. Survival outcomes in terms of DFS & OS were excellent. With clinical outcome data and dosimetric data of this study we recommend routine use interstitial brachytherapy if facilities are available and in clinical situations were ISBT is indicated.

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Funding and Conflict of Interest

The authors declare no conflict of interest. The study did not receive any funding.

Ethical Standards

This retrospective study was approved by Institutional Review Board and waiver of consent was obtained.

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