CONTENTS

EDITORIAL COMMITTEE

From the Editor's Desk

Postoperative pancreatic fistula: is a zero fistula rate achievable?

Dr Samir Bhattacharyya (Department of Surgical Oncology & Research)

Since the beginning of pancreas surgery, postoperative pancreatic fistula (POPF) has been the most important complication, and the major cause of postoperative mortality and morbidity. In recent years, the mortality following pancreatoduodenectomy (PD) has come down to approximately 2% in high volume centres (1). However, the morbidity rates after pancreatic resection still remain high at 30%-60% (2, 3). This assumes an increased importance in the context of PD for malignant disease. A prolonged period of morbidity can lead to delay in institution of, or even totally preclude, adjuvant therapy. This, in turn, can cause poorer outcome. Thus, a discussion on the issues pertaining to management of POPF is warranted.

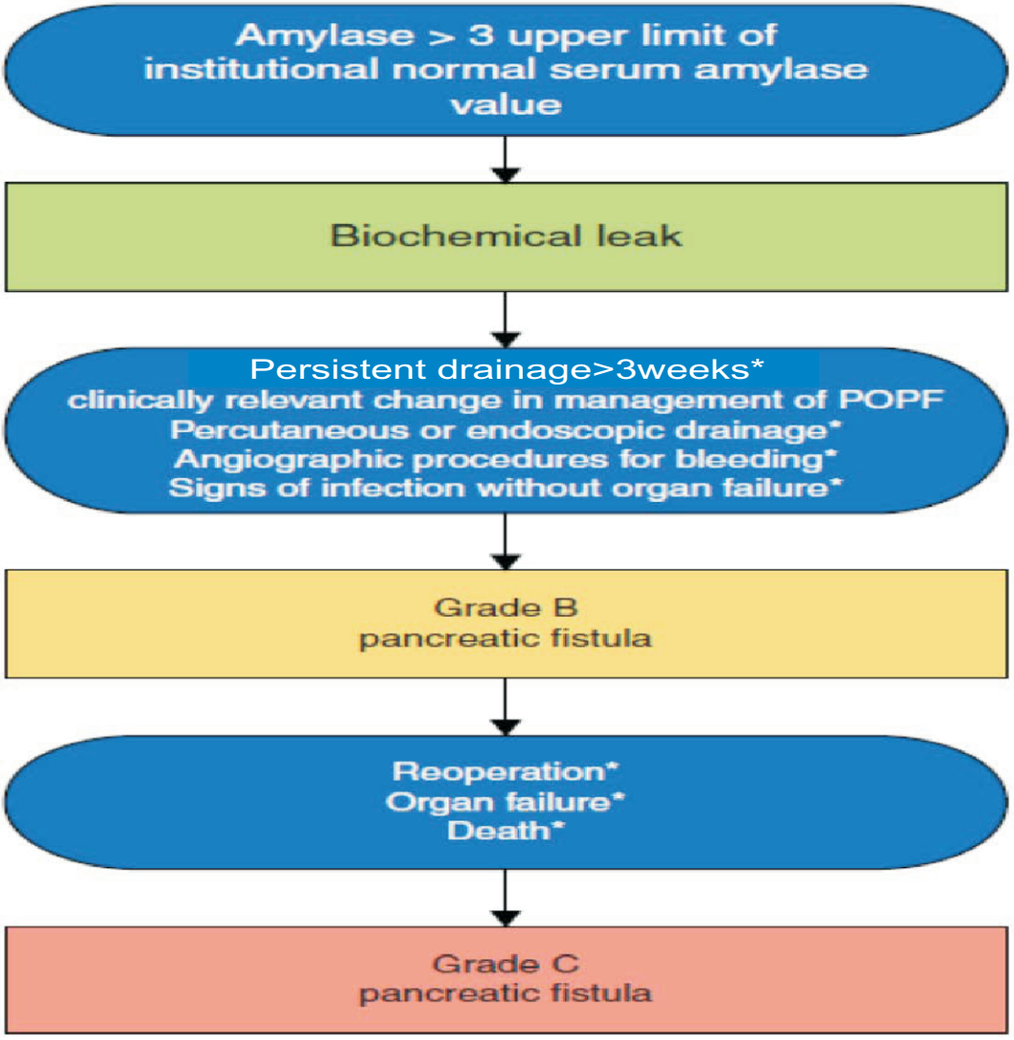
Pancreatic fistula has been defined as "an abnormal communication between the pancreatic ductal epithelium and another surface, where pancreas-derived, degradative, enzyme-rich fluid is evident." (4).

Before 2005, there was no generally accepted definition of POPF. In 2005, the International Study Group of Pancreatic Fistula (ISGPF) consensus statement, published on behalf of an international panel of recognized expert pancreatic surgeons presented a standardized definition of POPF. The panel defined POPF as "output via an operatively placed drain (or a subsequently placed, percutaneous drain) of any measurable volume of drain fluid on or after postoperative day 3, with an amylase content greater than 3 times the upper normal serum value." (4). The ISGPF subdivided POPF into three clinical grades, viz.

Grade A (biochemical leaks with little deviation from the normal clinical course, asymptomatic leaks only characterized only by an elevated drain amylase ie. 3 times the upper limit of normal serum amylase concentration).

Grade B and C fistulas are characterized by deviation from the expected clinical course, and often are a major source of morbidity. These are grouped together as clinically relevant fistulas (CR-POPF). Grade C fistulas are more severe than grade B and are characterized by at least one of three qualifiers: an operative intervention, some element of organ failure, or fistula-attributed death. CR-POPF contribute substantially to morbidity, mortality, and cost of care after PD. In 2017, the ISGPS modified the definition of POPF (Fig. 1) to exclude the clinically insignificant grade A category (5).

Fig 1. ISGPS 2016 POPF grades



Identification of patients at higher risk for development of POPF is essential in prevention and subsequent management strategies.

The Fistula Risk Score (FRS) is the most widely used and validated tool for risk stratification (6). It combines pancreatic parenchymal texture, disease pathology, pancreatic duct size, and intraoperative blood loss to stratify various risk groups (Table 1).

Table 1. Fistula Risk Score

Risk factor	Parameter	Points
Gland texture	Firm	0
	Soft	2
Pathology	Pancreatic adenocarcinoma or pancreatitis	0
	Ampullary, duodenal, cystic, islet cell, etc.	1
Pancreatic duct diameter	≥ 5 mm	0
	4 mm	1
	3 mm	2
	2 mm	3
	≤ 1 mm	4
Intraoperative blood loss	≤ 400 ml	0
	401–700 ml	1
	701–1000 ml	2
	>1000 ml	3
Total		0–10

The risk groups are as follows:

FRS 0: negligible
FRS 1–2: low
FRS 3–6: moderate
FRS 7– 10: high

How can we incorporate these in our clinical practice? Conceivably, a patient with negligible or low FRS and low drain fluid amylase (DFA) levels is not likely to develop POPF, and could benefit from no abdominal drainage or early removal of drain if placed. McMillan et al. reported in a trial, that early drain removal and selective drain placement was associated with improved outcomes in patients at low or negligible risk of POPF (7). Measurements of DFA levels to drive surgical drain management has been adopted in daily clinical practice and represents the standard of care.

Patients with high-risk features, on the other hand, need consideration of mitigation strategies such as, placement of abdominal drains, anastomotic stents, prophylactic somatostatin analogues, and modified anastomotic techniques. Ecker et al., in a large multicentric study, showed that in patients most vulnerable to the development of POPF, risk mitigation was best achieved by the combination of use of externalized stents and the omission of routine prophylactic octreotide, in association with pancreatojejunostomy (PJ) reconstruction (8). A recent RCT compared the POPF rates in patients at high risk of POPF after PJ or pancreatogastrostomy (PG), both with an externalized

transanastomotic stent. Though POPF rates were similar in both groups, PG was with an increased incidence of major morbidity. As such, PJ reconstruction was the recommended operative strategy with the use of an externalized stent in high-risk patients undergoing PD (9).
Modern risk-based management of surgical drains:

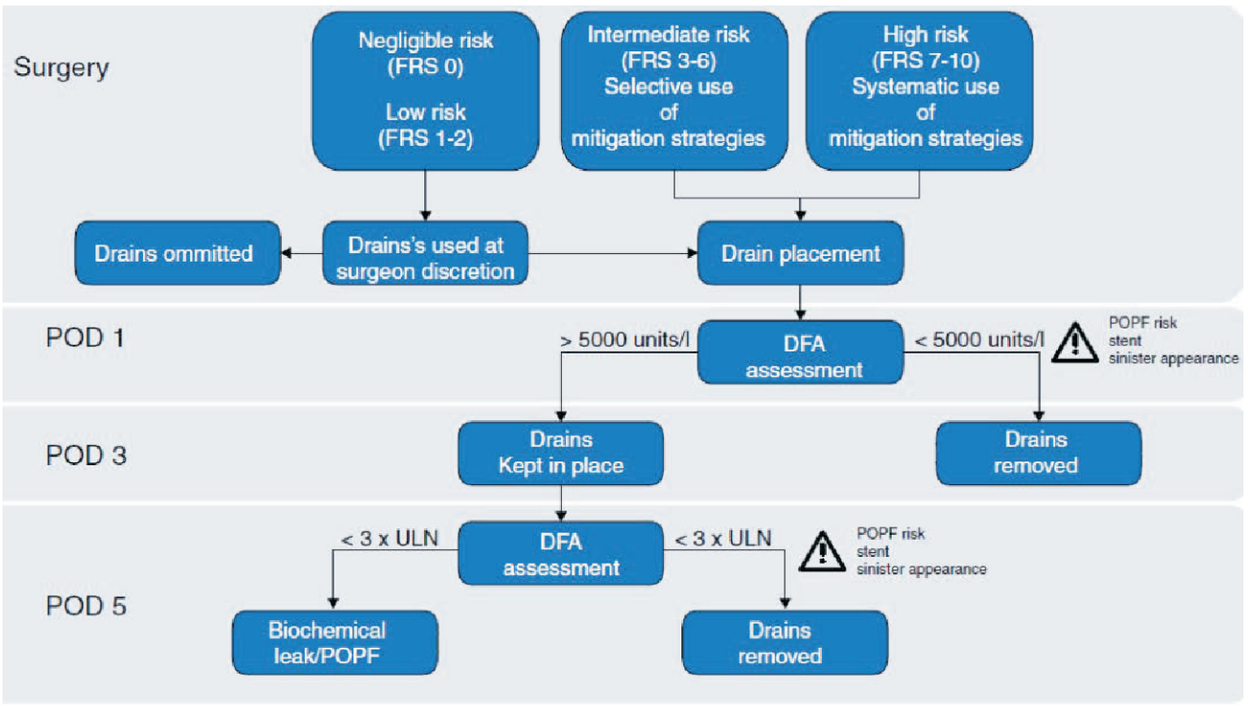
1. Low or negligible risk of fistula (FRS 0–2): drains are used at the surgeon's discretion and can be omitted. DFA level below 5000 units/l on POD 1 is considered an indication for early drain removal (POD 3). If the DFA level exceeds 5000 units/l on POD 1, or high-risk pancreatic features or an externalized transanastomotic stent are present, the DFA level is tested again on POD 5, and an amylase level exceeding three times the upper limit of normal used as cut-off to define the presence of biochemical leak/POPF.

2. Intermediate or high risk group: value of use of DFA thresholds are limited, as the evidences mostly were derived from outdated studies with methodological deficiencies (10). The utility of protocols for early drain removal based on DFA level remain questionable in these groups of patients, and DFA levels are rarely measured on POD 1 (11).

Thus, In the era of intraoperative risk stratification, it has become clear that a single protocol based on DFA concentration on POD 1 is not suitable for all clinical scenarios after PD.

A risk adapted approach towards drain management has been advocated recently (10) (Fig. 2).

Fig 2: Risk approach to drain management.



In conclusion, a zero fistula rate after PD seems unreal at present. However, a risk adapted approach to management can lead to a better outcome after this highly complicated surgery.

Reference:

1. Lewis R, Drebin JA, Callery MP, Fraker D, Kent TS, Gates J et al. A contemporary analysis of survival for resected pancreatic ductal adenocarcinoma. HPB 2013;15:49-60.
2. McMillan MT, Vollmer CM. Predictive factors for pancreatic fistula following pancreatectomy. Langenbecks Arch Surg. 2014;399(7): 811–24.
3. Vining CC, Kristine K, Darryl S, Pierce P, Yaniv B, Kevin KR, et al. Risk factors for complications in patients undergoing pancreaticoduodenectomy: a NSQIP analysis with propensity score matching. J Surg Oncol. 2020;122(2):183–94.
4. Bassi C, Dervenis C, Butturini G, Fingerhut A, Yeo C, Izbicki J, et al. Postoperative pancreatic fistula: an international study group (ISGPF) definition. Surgery. 2005;138(1): 8–13.
5. Bassi C, Marchegiani G, Dervenis C, Sarr M, Hilal MA, Adham M, et al. The 2016 update of the International Study Group (ISGPS) definition and grading of postoperative pancreatic fistula: 11 years after. Surgery. 2017;161(3): 584–91.
6. Callery MP, Pratt WB, Kent TS, Chaikof EL, Vollmer CM. A prospectively validated clinical risk score accurately predicts pancreatic fistula after pancreatoduodenectomy. J AmColl Surg2013;216:1–14.
7. McMillan MT, Malleo G, Bassi C, Allegrini A, Casetti L, Drebin JA et al. Multicenter, prospective trial of selective drain management for pancreatoduodenectomy using risk stratification. Ann Surg2017;265:1209–1218.
8. Ecker BL, McMillan MT, Asbun HJ, Ball CG, Bassi C, Beane JD et al. Characterization and optimal management of high-risk pancreatic anastomoses during pancreatoduodenectomy. Ann Surg2018;267:608–616.
9. Andrianello S, Marchegiani G, Malleo G, Masini G, Balduzzi A, Paiella S et al. Pancreaticojejunostomy with externalized stent vs pancreaticogastrostomy with externalized stent for patients with high-risk pancreatic anastomosis: a single-center, phase 3, randomized clinical trial. JAMA Surg2020;155:313–321.
10. Marchegiani G, Bassi C. Prevention, prediction, and mitigation of postoperative pancreatic fistula. Brit J Surg2021;108:602–604.
11. McMillan MT,Malleo G, Bassi C, SprysMH, Ecker BL, Drebin JA et al. Pancreatic fistula risk for pancreatoduodenectomy: an international survey of surgeon perception. HPB (Oxford) 2017;19.

----x-----

Original Article

Clinical Profile and Outcome of Patients Undergoing Autologous Stem Cell Transplantation following the second wave of Covid 19 pandemic - A Retrospective Study

Dr Partha Pratim Gupta, Dr Tusti Ganguly *(Department of Haematology Oncology & BMT)*

Introduction

Autologous stem cell transplantation (ASCT) is the standard consolidation therapy for newly diagnosed Multiple Myeloma patients who are eligible for the procedure [1, 2]. A number of randomized clinical trials [3] and meta-analyses [4] have shown that this approach is associated with improved progression free survival (PFS) and overall survival (OS) compared with conventional chemotherapy in patients with multiple myeloma. ASCT is also indicated for a variety of hematological malignancies like aggressive [5] and relapsed Non Hodgkin Lymphoma and relapsed Hodgkin Lymphoma [6] with chemotherapy responsive disease. The aim of this study is to present the outcome of autologous stem cell transplant (ASCT) program of our centre during ongoing covid 19 pandemic.

Patients and Methods:

The stem cell transplantation program was started in our Institute in January 2013. Covid 19 pandemic affected the hematopoietic stem cell transplant (HSCT) services worldwide including our centre too. Once the second wave of covid 19 was over, we restarted our HSCT program in June 2021. In this retrospective study, we analyzed the data of eleven patients with various hematological malignancies who underwent ASCT between June 2021 to September 2021.

Result

11 patients received autologous stem cell transplantation during this period. Among them, 8 (73%) were male and 3(27%) were female. The median age of this cohort was 56 years.(range 19-68). The study group consisted of newly diagnosed multiple myeloma(NDMM) 7, relapsed/refractory patients of multiple myeloma (RRMM) 2, relapsed Classical Hodgkin's Lymphoma (CHL) 1 and Mantle cell Lymphoma (MCL) 1. The predominant stage of multiple myeloma patients in this small study cohort was R-ISS II and IgG kappa was the commonest subtype followed by IgG lambda. Renal involvement was seen in 2 patients with multiple myeloma. The Hodgkin Lymphoma patient was of nodular sclerosis subtype who had early

relapse after first line ABVD therapy and achieved CR after 3 cycles of salvage chemotherapy with DHAP regimen. The MCL patient received sequential R-CHOP and R-DHAP for 8 cycles followed by Rituximab maintenance for 1 year prior to ASCT. All these patients received inj G-CSF 300 micrograms subcutaneously twice daily for 4 days and inj plerixafor 0.24mg/m2 on 4th day evening, 11 hours prior to commencement of stem cell harvesting. The median stem cell dose obtained with G-CSF +plerixafor mobilization was 11.8 million cells /kg (range 3.6 - 18).All patients of multiple myeloma was conditioned with melphalan chemotherapy. Among them 4 patients received melphalan at 200mg/m2, other 4 received melphalan at 140 mg/m2 and the remaining 1 patient of multiple myeloma who was 68 years old with renal amyloidosis received melphalan at 100 mg/m2 because of her frail overall general condition and impaired renal function with a raised serum creatinine of 2.3 mg /dl prior to transplant. The patients with relapsed Hodgkin Lymphoma and Mantle cell lymphoma received BEAM conditioning chemotherapy. All patients engrafted successfully and there was no transplant related mortality in this cohort. The median time to neutrophil engraftment was day +11(range d+9 to d+12) and the median time to platelet engraftment day was + 13 (range d+11 to d+17).All patients had regimen related toxicities. The most common toxicity was mucositis with grade I mucositis was seen in 100% of patients but only one patient had severe grade III mucositis, which persisted for 5 to 6 days. Mucositis was followed by diarrhea, anorexia and vomiting as the other regimen-related toxicities. The other major adverse events related to myeloablative conditioning chemotherapy was febrile neutropenia requiring broad spectrum intravenous antibiotic therapy in 8(73%) patients. The median duration of peri-transplant hospital stay was 29 days (range 23-44 days) and median duration of post-transplant hospital stay was 19 days (range 15-28 days).

Table : 1 - Profile of Patients undergone ASCT from June to September 2021

Case No.	Age	Sex	Diagnosis	Date of admission	Conditioning regimen	Cell dose (x10^6)	Date of ASCT	Date of discharge
1	42	M	RRMM	09-06-2021	MEL 200 TD 338	18	17-06-2021	05-07-2021
2	62	M	NDMM	21-06-2021	MEL 200 TD 350	12.6	29-06-2021	13-07-2021
3	56	M	NDMM	06-07-2021	MEL 140 TD 260	3.6	13-07-2021	31-07-2021
4	48	M	NDMM	09-07-2021	MEL 200 TD 320	5.54	15-07-2021	03-08-2021
5	62	M	NDMM	15-07-2021	MEL 140 TD 210	12.56	23-07-2021	10-08-2021
6	62	F	NDMM	04-08-2021	MEL 140 TD 200	17.73	11-08-2021	08-09-2021
7	19	F	Hodgkin Lymphoma	29-07-2021	BEAM	6.7	12-08-2021	31-08-2021
8	49	M	NDMM	23-08-2021	MEL 200 TD 330	11.8	01-09-2021	18-09-2021
9	54	M	Mantle Cell Lymphoma	27-08-2021	BEAM	6.17	14-09-2021	10-10-2021
10	68	F	NDMM with renal amyloidosis	03-09-2021	MEL 100 TD 140	6.8	10-09-2021	01-10-2021
11	65	M	RR MM	07-09-2021	MEL 140 TD 200	16.59	17-09-2021	06-10-2021

Discussion

Autologous Stem Cell Transplant (ASCT) plays a significant role in the management of hematologic malignancies. Indication and timing of transplant varies and depends on the type of disease we are dealing with. Like all other transplant centres across the globe [7], the

transplant program in our centre was also severely affected due to the ongoing covid 19 pandemic. We commenced our transplant activities in June 2021 after a gap of ten months. Since the average hospital stay during ASCT for a patient is around 4 weeks when they would have been exposed to all healthcare workers of the unit, our big concern was if they get covid 19 infection during this period. We strictly followed covid 19 protocols for all patients who had undergone ASCT and none of the patients in the study cohort got infected. There was no treatment related mortality (TRM) during this study period.

Conclusion:

ASCT can safely be performed in patients who are eligible for this modality of treatment during the current situation of covid pandemic, but strict adherence to covid 19 safety protocols has to be followed during the peritransplant period.

References

1. Kyle RA, Rajkumar SV. Multiple myeloma. Blood. 2008;111(6):2962–2972. doi: 10.1182/blood-2007-10-078022. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

2. Kumar L, Verma R, Radhakrishnan VR. Recent advances in the management of multiple myeloma. Nat Med J India. 2010;23(4):210–218. [PubMed] [Google Scholar]

3. Child JA, Morgan GJ, Davies FE, Owen RG, Bell SE, Hawkins K, et al. High-dose chemotherapy with hematopoietic stem-cell rescue for multiple myeloma. N Engl J Med. 2003;348(19):1875–1883. doi: 10.1056/NEJMoa022340. [PubMed] [CrossRef] [Google Scholar]

4. . Lévy V, Katsahian S, Fermand JP, Mary JY, Chevret S. A meta-analysis on data from 575 patients with multiple myeloma randomly assigned to either high-dose therapy or conventional therapy. Medicine. 2005;84(4):250–259. doi: 10.1097/01.md.0000173272.71949.a1. [PubMed] [CrossRef] [Google Scholar]

5. Autologous stem cell transplantation for mantle cell lymphoma – single

centre experience, Magdalena Szcześniak1, Anna Armatys1, Rafal Kurzawa1, Tomasz Kandzia1,Dominika Koziol1, Andrzej Frankiewicz1, Anna Kopinska2, Malgorzata

Krawczyk-Kulis2, Slawomira Kyrcz-Krzemien2, Grzegorz Helbig

6. Perales MA, Ceberio I, Armand P, et al. Role of cytotoxic therapy with hematopoietic cell transplantation in the treatment of Hodgkin lymphoma: guidelines from the American Society for Blood and Marrow Transplantation. Biol Blood Marrow Transplant 2015; 21:971.

7.COVID-19 pandemic and impact on hematopoietic stem cell transplantation, Kamal Kant Sahu, 1 Ahmad Daniyal Siddiqui,1 and Jan Cerny2

- x -

FREE FLAPS AT SGCCRI

Dr. Indranil Chatterjee, (ENT)
Dr. Shibshankar Paul, (ENT)
Dr Manish Kaushik,
(Department of Surgical Oncology)

Introduction

The primary challenge in surgically treating head and neck cancers, notably those that centrearound the upper aerodigestive tract is simultaneous maintenance of form and function to the best possible extent without compromising on the adequacy of extirpation.

Indian head and neck cancers are typically advanced in presentation. They come with additional concerns like resource constraints; stigmata associated with disease; accessibility issues where patients come from far-flung areas which hamper adequate follow-ups, early detection of recurrences or other issues that may hamper prognosis. Hence the choice of an adequate reconstructive option for a given patient, is not always textbook perfect in a high volume centre where patients come from all walks of life and are mostly resource poor.

A patient of squamous carcinoma of head and neck typically requires a primary surgery with or without additional reconstruction which most often needs to be followed up by adjuvant treatment in the form of radiotherapy and chemotherapy- in isolation or combination. There is a specific time frame that needs to be adhered to, failing which prognosis(outcome in common language) may be affected. Hence resource allocation also needs to be kept in mind so as to fit-in the entire treatment without jeopardizing outcome.

Head and neck houses the six senses and twelve cranial nerves- which bring in major concerns of function, as this is the area that manifests the individual's persona. Oral cancers- which form a major chunk of such cancers come with major concerns of 'intelligible' speech, feeding and taste perception. Lower down the pharynx and larynx bring in concerns of airway and food-passage co-ordination and voice itself inaddition to the above. Cosmesis is a generalized concern in all head and neck cancers. A major cosmetic concern is the continuity of the jawline which is often hampered by mandibular resection.

Selection of appropriate reconstructive option for an individual with oral squamous carcinoma thus 'ideally' is supposed to be one that maximizes outcome yet causes minimum morbidity, promotes fast post-surgery recovery with minimal complications. From this point of view, the world over, microvascular free tissue transfer is the gold standard method adopted.

At Saroj Gupta Cancer Centre and Research Institute, the Head and Neck Unit has been undertaking microvascular reconstruction in suitable cases after due consideration of patient expectations, adequate counseling of available options of reconstruction for individual cases and other logistics- all with a wholesome outlook of optimizing treatment outcome. The Institute

is a unique blend of a Private Trust run Centre with philanthropic outlook- therefore cost optimization of treatment definitely has a role to play, specially with a significant proportion of patients having fund issues. Hence, majority of patients receive pedicled flaps like Pectoralis major, latissimusdorsi or other simpler reconstructions. Free flaps are reserved for mandible sparing lesions, or locally advanced resectable disease where resurfacing warrants significant amount of tissue cover.

We have been undertaking such cases on a regular basis since December 2018, backed by a skilled Plastic Surgery team who make themselves available for the cases. The free flaps are routinely performed by plastic surgeons, who are more attuned to the nuances and challenges of such reconstruction and deliver single shot outcomes. The Institute runs a DNB Superspeciality program in Oncosurgery and such work provides a unique opportunity for trainees to imbibe the broad principles of balancing an adequate resection and reconstruction with hands-on experience.

Our Experience

In our initial days we have taken care to select patients with minimal co-morbidities, or those with co morbidities under control. Locally advanced yet resectable cancers have been prioritized, more so in younger age groups who are expected to fare better in the post-surgical period. Three major flaps are seen to cover most of the head and neck defects- the radial forearm fasciocutaneous, the anterolateral thigh myofasciocutaneous and the fibular flap.

We present highlights of our brief experience in handling such cases in the ensuing paragraphs.

1. Number of patients:In all, we had 35 patients who underwent microvascular reconstruction following head and neck resection in the period 2019 to 2021. There was a sharp decline in cases during 2020 owing to the COVID 19 pandemic, and although cases picked up in early 2021, the second wave led to a dip in cases. This explains our humble numbers as of now.
2. Primary Site: Being oral cancers, we see that almost 85 % of our cases receiving free flaps were involving the buccal mucosa with and without the gingival regions. One female patient of tongue with floor of mouth (AJCC IVA) involvement received a radial forearm flap, and is doing well almost one year post surgery. 8% involved the upper alveolus and maxilla and received a free flap.
3. Histology: 8% of the cases were documented as extensive verrucous lesions after detailed histological examination. Rest were squamous cell carcinomas, except one which was an angiosarcoma.
4. Stage of disease: Stagewise, the pathological stage reflected close to 55%(20 out of 36) of the cases operated as belonging to AJCC stage IV of which 1/5th were stage IVB. Approximately 35% were of stage III.
5. Type of flap:26 patients received radial forearm flaps. 10 patients received anterolateral thigh flaps. Fibular reconstruction was discussed with several patients, but when

specifically told that there will be further costs involved in full restoration of chewing function with dental implants, cost of plates during the flap surgery and so forth, most opted for the ALT or the simple option of peducled PMMC. Just the restoration of jawline did not seem to be the primary concern of the category of patients we have handled.

6. Complications:Complications included minor wound infections and seromas in a negligible proportion of cases. Flap margin necrosis especially of those anchored to the upper gingival margin was noticed in 2 cases. Desquamation was noted in 2 cases, not needing any active measures. They healed spontaneously with postural adjustments and supportive medications. Flap oedema during the first 48 hours was noted but subsided spontaneously. Tracheostomy is practiced routinely to negate the potential hazard of aspiration related events immediately post operatively and also has been observed to keep the patient calm despite having a bulky tissue implant in their oral cavity. They are typically weaned off by 4th to 5th day. An elderly obese female patient of extensive lower lip and central jaw disease, who had received an ALT, but was tolerating the surgery poorly developed flap thrombosis 48 hours post surgery which could not be salvaged. A PMMC was performed. She however succumbed due to sudden cardiac arrest a day later.
7. Donor site morbidity was minimal in all cases. All Radial forearm donor sites were covered with Split skin grafts and no primary closure was attempted. ALT flaps did not pose any such issue.
8. The average hospital staypost surgery was 8-10 days. Most patients were out of bed and ambulatory by 5th day. Nasogastric tubes are routinely kept in-situ for at least one week post surgery.
9. Adjuvant Therapy: Barring those with verrucous carcinoma, all patients were advised adjuvant radiotherapy based on final histology. Out of 36, 3 patients defaulted after surgery. The rest received radiotherapy. One patient succumbed to Type II Respiratory failure during his radiotherapy period.
10. Lost to Follow Up:Significantly, the impact of COVID 19 is felt in this small volume of cases as well, in the form of absent follow up of 6 post treatment patients who were on follow up pre COVID.
11. Recurrence:So far we have identified 5 cases with documented recurrence, of which 3 patients have died.
12. Mortality that has been so far documented is 5, i.e.14%. This includes one immediate post-operative death and one during radiotherapy.

Summary

Our experience in regularly performing such cases is pretty much at a nascent stage and has been hit by the two year long COVID pandemic. However, as the entire team rides the mandatory learning curve, what we have gained is a trained team of doctors and supporting OR, ITU and ward staff who should know the SOP well when it comes to handling these cases. What we upheld in the preceding paragraphs was just a snapshot of our brief experience and to

4. Ibid.

come up with any tangible comment will need a much higher volume of cases which we expect to amass in due course of time.

Another comment worth making is, we notice that lack of treatment adherence and follow up, often unexplained, is a serious problem in our set of patients, which hampers the completeness of therapy and also follow-up data. Ensuring proper and timely adherence to adjuvant therapy and early detection of recurrences facilitated by a stringent follow up regimen is the key to establishing the success of a sensible resection-reconstruction endeavor in head and neck cancers.

ADVANCED RADIOTHERAPY TECNIQUES & SGCCRI

DR JYOTIRUP GOSWAMI
(Department of Radiation Oncology)

Introduction to modern radiotherapy techniques:

Modern Radiotherapy Techniques

- IMRT (Intensity Modulated Radiotherapy)
- VMAT (Volume Modulated Arc Therapy)
- IGRT (Image Guided Radiotherapy)
- SRS/SRT (Stereotactic Radiosurgery & Radiotherapy) [Cranial]
- SBRT (Stereotactic Body Radiotherapy)

How do Modern Radiotherapy Techniques optimise cancer outcomes?

- By providing superior toxicity profile in existing successful treatment settings, eg IMRT reduces xerostomia (dryness of mouth) in head-neck cancer
- By enabling superior tumor control in existing treatment settings, eg IMRT & IGRT enable dose escalation in prostate cancer, leading to superior disease control
- By providing disease control solutions in innovative treatment settings, eg SBRT for hepatocellular carcinoma

IMRT

- Is a form of treatment delivery to achieve highly conformal dose distribution, ie treatment dose fits on the target & spares normal tissue as far as possible
- Uses complex dose prescription techniques, called Inverse Planning, whereby the physician is able to specify desired dose-constraints to the target & normal tissues

Parotid dose ,xerostomia& IMRT

- With conventional radiotherapy in head-neck cancer, all patients undergo irradiation of parotid glands to a high dose, leading to irreversibly damaged function: this leads to permanent dryness of mouth
- Research has shown Severe xerostomia (<25% of baseline) can be avoided if mean parotid dose is kept to <20Gy (if one parotid is to be spared) or <25 Gy(if both are to be spared)
- IMRT enables parotid sparing and reduces the possibility of long-term xerostomia.
- Thus patients are able to achieve complete recovery of salivary function, facilitating better swallowing & speech functions, hence allowing for a better quality of life
- Research has also established that sparing of the parotid glands does not negatively impact tumor control.

IMRT for prostate cancer

- Radical radiotherapy is the curative option for organ-confined prostate cancer
- Radiotherapy dose escalation has been shown to improve disease control rates
- IMRT allows RT dose escalation while controlling doses to the adjacent anterior wall of the rectum
- Thus, IMRT in prostate cancer enables superior disease control with tolerable toxicity profile (rates of late radiation proctitis, causing bleeding per rectum are <5%)

IMRT & VMAT

- The linear accelerator treatment head has an array of small blocks called Multi-Leaf Collimators (MLCs).
- During IMRT delivery, the MLCs shape the beam aperture in a combination of different irregular shapes. Delivery is comparatively slower at 15-20 minutes.
- VMAT is a more sophisticated form of IMRT, where not only is treatment more focused but it allows comparatively much faster treatment delivery , within 2-2.5 minutes.
- Faster treatment minimises patient movement & maximises comfort.

IGRT

- Image guided radiotherapy is a broad concept whereby frequent imaging is done in the treatment room for more accurate treatment delivery.
- IGRT is mainly to ensure accurate patient positioning and overcoming problems due to organ motion.
- Due to variations in patient setup & organ motion, an extra margin of tissue has to be radiated to deliver adequate dose to the tumor
- IGRT can help us to eliminate or at least, reduce this margin
- This results in much less normal tissue being irradiated to high doses

Stereotactic radiotherapy

- Refers to extremely accurate localisation of a point in space
- Stereotactic radiotherapy refers to a technique of extremely focused radiotherapy
- It is usually delivered in a small number of fractions (1-5), with large dose/fraction (>4Gy/#), unlike conventional radiotherapy which is delivered in small doses over a long time (1.8-2Gy/#, once a day, 5 days a week for 5-7 weeks).
- Delivering a much higher dose over a shorter course of time, allows the radiation to be more effective biologically.
- The effect of stereotactic radiotherapy is akin to surgery.
- Stereotaxy was first achieved in cranial lesions, many of them benign, eg arterio-venous malformations, craniopharyngioma, pituitary adenoma & acoustic neuroma
- These all feature treatment of a small target, adjacent to vital areas, to a dose much higher than the tolerance dose of nearby structures.
- Stereotactic radiotherapy is today, also the preferred treatment modality for brain metastases. It has been shown to be equivalent to surgery or whole brain radiotherapy.
- The first machine to deliver stereotactic radiotherapy was the Gamma knife, created by Lars Leksell (a neurosurgeon) in 1961. This machine uses 201 small telecobalt sources.
- Today, cranial stereotaxy can also be delivered by specially equipped linear accelerators (the so-called X-knife)
- Cranial stereotaxy initially was based on physically & invasively fixing a rigid frame to the patient's cranium.
- The frame was required for the accurate localisation of the target on imaging.
- In the modern day, we have come to use non-invasive frames.
- Use of sophisticated pre-treatment imaging, such as in-room Cone Beam CT, has allowed us to do away with frames altogether.

SBRT

- Also called Stereotactic Ablative Body Radiotherapy (SABR)
- Extracranial stereotaxy has become possible because of Image Guidance in the treatment room
- SBRT is done for tumors of the lung, liver, pancreas, prostate & spine.
- SBRT is the most exciting recent development in lung cancer therapy.Early lung cancers, though rare, are curable by surgery.However, many such patients have severe COPD & other medical comorbidities, precluding surgery.SBRT has provided an alternative to these patients.It has been shown to be as effective as surgery for local control.
- SBRT to the liver/lung metastases achieves superior local control, as compared to using systemic therapy (chemotherapy) alone
- More feasible than surgery for patients with poorer performance status / with less accessible lesions

The Story of Modern Radiotherapy at SGCCRI:

- At SGCCRI, Thakurpukur, we have been installing our new state-of-the-art linear accelerator, the Varian Vital Beam, capable of IMRT, IGRT , SRS and SBRT.
- A linear accelerator is a very sophisticated piece of equipment, with many many moving parts and complex computer-controlled components.
- Installing a linear accelerator is no small matter!
- Firstly, a special room with thick concrete walls had to be constructed. The shielding is to prevent leakage of radiation outside.
- Work was concluded late-September 2021
- Then, the equipment arrived in massive shipments, the hardware mostly from USA and the software mostly from Europe, in mid-September 2021.
- Once the bunker was made dust-free & all electrical & civic work completed, the boxes were unpacked and the equipment was pieced together, to physically instal the linear accelerator.
- This started on 18th October 2021.
- Then the sophisticated wires and circuits are installed.
- This work started at end-October 2021 & completed in a weeks' time.
- After this, the installation team did a survey of the entire premises to check that the bunker was not leaking radiation.
- Once this was deemed satisfactory by the Atomic Energy Regulatory Board, the machine was turned on.

- Before clinical treatment can begin, there is a lengthy process of calibration of the different radiation beams, known as Commissioning, to ensure that the machine is capable of delivering radiotherapy as per standard.
- We started clinical treatment by mid- February 2022.

Components:

- Photon beams-6MV & 15MV
- Unflattened photon beam-6X
- Electron beams-6 energies
- 120-leaf Millenium MLCs
- High Dose Rate mode
- Electron Portal Imaging Device
- On-Board Imager

Capabilities:

- Conventional RT
- 3D conformal RT
- Electron Beam therapy
- IMRT
- Rapid Arc
- IGRT (2D-KV,2D-MV,3D)
- TBI
- TSET
- SRS/SRT (cranial)
- SBRT

Our Journey in Brachytherapy:

We have also installed a new Brachytherapy machine-the Elekta Flexitron- Cobalt.

Features:

- Uses miniaturised Cobalt-60 source
- Dosimetrically identical to Iridium-192 for most purposes
- Long half-life 5.26 years greater affordability

Capabilities:

- Intracavitary brachytherapy (gynaecological cancers)
- Interstitial brachytherapy (gynaecological cancers/ breast cancer/ prostate cancer/soft tissue sarcoma)
- Intraluminal brachytherapy (lung cancer/oesophageal cancer)
- Surface mould (skin cancer)

CCWHRI / SGCCRI Hospital Cancer Registry 1996-2020

Dr Jyotirup Goswami, Dept. of Radio therapy

Salient points:

- Years covered=25
- 1996-2020
- Total patients=1,89,315
- Average patients/ year=7572
- Evaluated in individual years & 5-year blocks
- 1996-2000, 2001-2005, 2006-2010, 2011-2015, 2016-2020

Interesting trends:

- Consistent rise in oral cavity cancers & lung cancer in males
- Consistent rise in breast cancer & ovarian cancers in females
- Consistent fall in other head-neck cancers & cervical cancers
- Consistent rise in number of hematological malignancy cases
- Breast cancer has now overtaken cervical cancer in the mid-2000s as the leading cancer in women.
- Slight decrease in the relative incidence of cervical cancer cases presenting in advanced stage (III) vs early stage (I/II)
- Digestive cancers have doubled over the last 25 years.
- The commonest digestive cancers are stomach cancer & colorectal cancers.
- The incidence of stomach cancers has increased quite steeply.
- Oesophago-gastric & hepatobiliary cancers have been more common in women, while colorectal & pancreastic cancers have been more common in men.

Effect of Covid:

- Patients in 2020=4031
- Caused by lockdown & difficulty of access
- As a result, some of the trends in the 5-year period 2016-2020 are somewhat blunted (though not reversed)
- The disease outcomes for patients during this period are likely to be inferior due to delayed diagnosis and workup

75 Successful Bone Marrow Transplantation Eight Year Journey of Autologous Haematopoietic Stem Cell Transplant Program of Saroj Gupta Cancer Centre & Research Institute

Dr Partha Pratim Gupta, Dr Rabindra Nath Ghosh
(Department of Haematology Oncology & BMT)

Introduction:

Bone Marrow Transplant also known as Haematopoietic Stem Cell Transplant (HSCT) is a procedure that involves the intravenous infusion of healthy haematopoietic cells to reestablish normal haematopoiesis in patients with dysfunctional or depleted bone marrow. First explored in humans in the 1950s by Dr Thomas, hematopoietic stem cell transplantation is now used worldwide in the treatment of many malignant and non malignant haematologic conditions and in the treatment of various solid tumors.

HSCT is of two types; i) Autologous Transplant in which patients own stem cell is infused to reestablish bone marrow function following high dose therapy (HDT) and ii) Allogeneic Transplant where stem cell is obtained from a HLA matched healthy donor to restore normal haematopoiesis in patients whose bone marrow function is defective.

Multiple Myeloma is the most common indication for autologous stem cell transplantation (ASCT) followed by Non Hodgkin's and Hodgkin's Lymphoma and Acute Myeloid Leukemia, solid tumors like Neuroblastoma and Germ Cell Tumor and certain non malignant diseases such as Autoimmune Disorders like SLE and Multiple Sclerosis.

In our centre, Autologous Transplant Programme has been started since January 2013. We are hereby giving a brief update of the 75 Autologous HSCT done so far at our centre for various Haematological Malignancies.

Materials and Methods:

Total of 75 patients of which 60 patients had Multiple Myeloma; six patients had Relapsed Non Hodgkin's Lymphoma (DLBCL) seven patients with relapsed Hodgkin Lymphoma and one each with Plasma Cell Leukemia and Acute Promyelocytic Leukemia who received Autologous HSCT between January 2013 and October 2021.

Central venous access devices

Central venous line was done in all patients, either a peripherally inserted central catheter (PICC) or a subclavian/jugular venous line was done for IV access for the peritransplant period except for one patient, who had a chemoport inserted during salvage chemotherapy. Peripheral Blood Stem Cell apheresis was done through a femoral line. This femoral catheter was inserted on the day before the apheresis procedure and was removed on day 0, following infusion of stem cells through this line.

Stem cell mobilization, apheresis and storage

Our peripheral blood stem cell (PBSC) mobilization protocols were 1) G-CSF alone 2) G-CSF plus chemotherapy and 3) G-CSF plus Plerixafor. Mobilization strategy used was G-CSF 5 microgram per kg per dose twice daily for 4 days following which on the 5th day after the morning dose of G-CSF; patients underwent peripheral blood stem cell (PBSC) apheresis using either COBE spectra or Spectra

Optia auto PBSC Apheresis System. When plerixafor was used, it was given along with G-CSF at the recommended dose of 0.24 mg / kg eleven hours before commencement of apheresis procedure. The target cell dose was 2.5 X 10^6 cell/kg. Patients not achieving the target cell dose were continued on mobilization and underwent apheresis on the second day as well. After apheresis, the PBSC products were stored at 4^0 C in a blood bank refrigerator up to 48 h for multiple myeloma patients The PBSC products were cryopreserved and stored at -90^0 C freezer for all patients of lymphoma and the APL patient because the administration of BEAM and BuCy conditioning chemotherapy requires 6 days and 4 days respectively. 24 hours post conditioning chemotherapy, the entire PBSC product was infused to the patient using a regular blood transfusion set. Depending on the volume, the infusion process was completed in one or two sittings to avoid volume overload.

Conditioning chemotherapy

The myeloablative conditioning regimen used for Multiple Myeloma patients was single agent melphalan in doses ranging from 200 mg/m², 140 mg/m² or 100 mg/ m². Dose adjustment of Melphalan was done based on age of the patient, performance status (fit vs frail) and associated comorbidities esp. CKD at the time of transplant. BEAM was utilized as a conditioning chemotherapy for the majority of patients with NHL and Hodgkin Lymphoma and only one patient with HL received BACE as conditioning chemotherapy, the Plasma Cell Leukemia patient received high dose melphalan @ 200 mg/m² and the APL patient received Busulfan-Cyclophosphamide(BuCy) conditioning chemotherapy.
Supportive care and Monitoring

All patients were admitted to an isolation room of our 4 room BMT unit. Each room has a terminal HEPA filter with positive air pressure facilities. Barrier nursing protocol was also followed strictly. Acyclovir and fluconazole were given as prophylaxis for HSV and fungal infections respectively to all patients as per our protocol. No antibacterial prophylaxis was used routinely. To hasten recovery of neutrophil count, G-CSF was routinely started from Day +4. Neutrophil engraftment was defined as the first day of absolute neutrophil count (ANC>500) for three consecutive days. The date for platelet engraftment was considered the posttransplantation day of platelet achievement of >20 X 10^9 /L for 3 days without component support.

Result:

The age of the patients ranged from 15 years to 69 years (median 54 years) with male : female ratio of 1.7:1. The median peripheral blood stem cell dose was 5.7x10^6 CD34+ve cells/kg (range 2.3456.9x10^6 CD34+ve cells / kg). Adequate peripheral blood stem cell mobilization was possible with G CSF alone in 33 patients, chemotherapy followed by G-CSF in one patient, chemotherapy plus G-CSF plus plerixafor in three patients and for the remaining 38 patients, plerixafor along with G-CSF was used as the mobilization protocol for apheresis of desired minimum stem cell dose. Eighty percent of patients had one sitting and the remaining 20% of patients had to undergo another sitting of apheresis on the second day to achieve target stem cell dose. The median time to neutrophil engraftment was 11 days (range 9 - 13) and the median time to platelet engraftment day was 14 days (range 11 -17). Table 1 shows the patients characteristics and minimal outcome data of our transplant patients.
Regimen related toxicity was seen in all patients. The most common toxicity was mucositis with grade I mucositis was seen in 100% of patients but only around one fifth of them had severe grade III mucositis,

necessitating TPN support for 5 to 6 days. Mucositis was followed by diarrhea, anorexia and vomiting as the other regimen-related toxicities. The major adverse event related to myeloablative conditioning chemotherapy was febrile neutropenia requiring broad spectrum intravenous antibiotic therapy in almost three fourth of all patients. Serial blood and urine cultures and monitoring of inflammatory markers were routinely done during febrile episodes. The most common isolates were Gram negative organisms (Klebsiella Sp. and E coli). Staph aureus was the most common Gram positive organism. Though all patients received oral fluconazole prophylaxis, requirement for the use of intravenous antifungal therapy was minimal and were limited to caspofungin and amphotericin B deoxycholate. The median duration of peri-transplant hospital stay was 29 days (range 23-84 days) and median duration of post-transplant hospital stay was 19 days (range 15-70 days).

Table 1- Patient characteristics and Minimal outcome data

SNO	Year	Date of transplant	Diagnosis	Disease type	Cond Regimen	Age	Sex	Date of LFU/Death	Time (days)	Status
		mm/dd/yyyy				Year	M-1 F-2	mm/dd/yyyy		Dead-1 Alive-0
1	2013	23-01-2013	MM	PCD-Myeloma	MEL 200	45	1	17-12-2019	2519	1
2	2014	16-01-2014	NHL	Mature B cell lymphoma	BEAM	40	1	24-05-2014	128	1
3	2014	09-02-2014	MM	PCD-Myeloma	MEL 200	59	1	06-08-2018	1639	1
4	2014	12-04-2014	MM	PCD-Myeloma	MEL140	65	2	24-02-2015	318	1
5	2014	22-04-2014	MM	PCD-Myeloma	MEL 200	54	2	19-02-2021	2495	0
6	2014	11-07-2014	PCL	PCD-Myeloma	MEL 200	58	2	01-12-2014	143	0
7	2014	16-07-2014	MM	PCD-Myeloma	MEL140	66	1	28-01-2020	2022	0
8	2014	06-08-2014	MM	PCD-Myeloma	MEL 200	49	1	09-11-2016	826	1
9	2014	07-08-2014	MM	PCD-Myeloma	MEL140	75	2	17-03-2021	2414	0
10	2014	17-09-2014	MM	PCD-Myeloma	MEL 200	56	2	15-09-2016	729	0
11	2014	25-11-2014	MM	PCD-Myeloma	MEL 200	54	1	04-02-2020	1897	0
12	2014	08-12-2014	NHL	Mature B cell lymphoma	BEAM	56	1	16-10-2020	2139	0
13	2014	24-12-2014	MM	PCD-Myeloma	MEL 200	56	1	19-04-2019	1577	0
14	2015	21-01-2015	MM	PCD-Myeloma	MEL140	63	1	04-02-2020	1840	0
15	2015	07-04-2015	NHL	Mature B cell lymphoma	BEAM	45	1	30-09-2015	176	0
16	2015	24-04-2015	MM	PCD-Myeloma	MEL 200	68	2	16-03-2021	2153	0
17	2015	16-06-2015	MM	PCD-Myeloma	MEL 200	47	1	24-05-2019	1438	1
18	2015	28-09-2015	HL	Hodgkin Lymphoma	BEAM	59	2	13-04-2017	563	0
19	2015	01-12-2015	MM	PCD-Myeloma	MEL140	63	2	05-01-2021	1862	0

20	2015	04-12-2015	MM	PCD Myeloma	MEL 200	45	1	27-12-2016	389	0
21	2015	26-12-2015	MM	PCD-Myeloma	MEL 200	65	1	02-02-2019	1134	0
22	2015	29-12-2015	MM	PCD-Myeloma	MEL 200	65	2	17-01-2020	1480	0
23	2016	02-02-2016	MM	PCD-Myeloma	MEL 200	53	2	28-07-2017	542	0
24	2016	10-02-2016	MM	PCD-Myeloma	MEL 200	62	1	12-03-2021	1857	0
25	2016	30-03-2016	MM	PCD Myeloma	MEL 200	60	1	04-03-2021	1800	0
26	2016	18-05-2016	MM	PCD-Myeloma	MEL 200	59	2	04-02-2020	1357	0
27	2016	15-06-2016	MM	PCD-Myeloma	MEL 200	62	1	04-02-2020	1329	0
28	2016	20-10-2016	MM	PCD-Myeloma	MEL-200	57	2	16-03-2020	1243	0
29	2016	11-11-2016	MM	PCD-Myeloma	MEL 200	40	1	14-02-2017	95	1
30	2016	22-11-2016	MM	PCD-Myeloma	MEL 200	50	1	04-02-2020	1169	0
31	2016	13-12-2016	MM	PCD-Myeloma	MEL 200	66	2	11-02-2020	1155	0
32	2017	02-01-2017	APML	AML non 1st CR	BuCy	34	1	12-03-2021	1530	0
33	2017	14-01-2017	MM	PCD-Myeloma	MEL-200	49	2	07-08-2017	205	1
34	2017	02-02-2017	MM	PCD-Myeloma	MEL-140	54	2	11-02-2020	1104	0
35	2017	23-02-2017	MM	PCD-Myeloma	MEL-200	46	1	17-08-2018	540	0
36	2017	11-05-2017	HL	Hodgkin Lymphoma	BEAM	30	1	23-12-2020	1322	0
37	2017	26-05-2017	MM	PCD-Myeloma	MEL-200	44	1	16-03-2019	659	0
38	2017	31-05-2017	HL	Hodgkin Lymphoma	BEAM	13	1	04-02-2020	979	0
39	2017	22-07-2017	MM	PCD-Myeloma	MEL-140	49	2	15-06-2019	693	1
40	2017	04-08-2017	MM	PCD-Myeloma	MEL-200	45	2	04-02-2020	914	0
41	2017	08-08-2017	MM	PCD-Myeloma	MEL-200	50	2	04-02-2020	910	0
42	2017	05-09-2017	MM	PCD-Myeloma	MEL-200	49	2	10-02-2021	1254	0
43	2017	19-12-2017	MM	PCD-Myeloma	MEL-140	70	1	17-03-2021	1184	0
44	2018	16-02-2018	MM	PCD-Myeloma	MEL-200	64	2	06-03-2021	1114	0
45	2018	21-02-2018	MM	PCD-Myeloma	MEL-200	57	1	21-11-2019	638	0
46	2018	18-05-2018	HL	Hodgkin Lymphoma	BEAM	54	1	24-05-2018	6	1
47	2018	14-08-2018	MM	PCD-Myeloma	MEL-200	56	1	21-10-2019	433	0
48	2018	28-09-2018	MM	PCD-Myeloma	MEL -200	51	2	12-02-2020	502	0
49	2018	21-11-2018	HL	Hodgkin Lymphoma	BEAM	20	1	04-02-2020	440	0
50	2018	07-12-2018	MM	PCD-Myeloma	MEL-140	65	1	04-04-2019	118	0
51	2019	09-01-2019	MM	PCD-Myeloma	MEL- 200	45	1	18-03-2021	799	0
52	2019	12-03-2019	MM	PCD-Myeloma	MEL- 200	64	1	16-05-2020	431	0
53	2019	20-03-2019	MM	PCD-Myeloma	MEL-140	49	1	17-02-2021	700	0

54	2019	17-07-2019	NHL	Mature B cell lymphoma	BEAM	41	2	25-02-2020	223	0
55	2019	09-08-2019	MM	PCD-Myeloma	MEL- 200	42	1	10-03-2021	579	0
56	2019	12-09-2019	MM	PCD-Myeloma	MEL- 200	51	2	17-03-2021	552	0
57	2019	22-10-2019	MM	PCD-Myeloma	MEL- 200	58	2	17-06-2020	239	0
58	2019	19-11-2019	MM	PCD-Myeloma	MEL- 200	45	1	04-02-2020	77	0
59	2019	27-12-2019	MM	PCD-Myeloma	MEL- 200	58	1	20-02-2020	55	0
60	2020	01-01-2020	MM	PCD-Myeloma	MEL - 200	68	1	08-03-2021	432	1
61	2020	12-02-2020	MM	PCD-Myeloma	MEL - 200	39	2	08-03-2021	390	1
62	2020	19-02-2020	MM	PCD-Myeloma	MEL - 200	45	1	18-01-2021	334	0
63	2020	16-09-2020	HL	Hodgkin Lymphoma	BEAM	14	1	23-09-2020	7	1
64	2020	26-11-2020	MM	PCD-Myeloma	MEL-200	44	1	12-03-2021	106	0
65	2012	17-06-2021	MM	PCD-Myeloma	MEL-200	42	1	24-12-2021	190	0
66	2021	29-06-2021	MM	PCD-Myeloma	MEL-200	62	1	30-11-2021	154	0
67	2021	13-07-2021	MM	PCD-Myeloma	MEL-140	56	1	21-12-2021	161	0
68	2021	15-07-2021	MM	PCD-Myeloma	MEL-200	48	1	21-12-2021	159	0
69	2021	23-07-2021	MM	PCD-Myeloma	MEL-140	62	1	17-12-2021	147	0
70	2021	11-08-2021	MM	PCD-Myeloma	MEL-140	62	2	22-11-2021	103	0
71	2021	12-08-2021	MM	Hodgkin Lymphoma	BEAM	19	2	29-11-2021	109	0
72	2021	01-09-2021	MM	PCD-Myeloma	MEL-200	49	1	29-11-2021	89	0
73	2021	10-09-2021	MM	PCD-Myeloma	MEL-100	68	2	21-12-2021	102	0
74	2021	14-09-2021	MCL	Mature B cell lymphoma	BEAM	54	1	06-12-2021	83	0
75	2021	17-09-2021	MM	PCD-Myeloma	MEL-140	65	1	17-12-2021	91	0

MM-Multiple Myeloma, NHL-Non-Hodgkin Lymphoma, HL-Hodgkin Lymphoma, PCL-Plasma Cell Leukemia, APML-Acute Promyelocytic leukemia, MCL-Mantle Cell Lymphoma, PCD-Plasma Cell Dyscrasia, MEL-Melphelan, BEAM-quadruplet conditioning chemotherapy, BucY- Busalphan-Cyclophosphamide

Conclusion:

Autologous stem cell transplant remains a necessary component of therapy in various haematologic disorders, especially in the management of Myeloma and Lymphoma patients. In Multiple Myeloma, even in the era of novel agents, ASCT adds to the benefit obtained from proteasome and immunomodulatory drug based induction therapy in terms of both PFS and OS. The use of HDT with autologous rescue remains very important in the treatment of R/R Lymphoma. Our limited follow up data is really encouraging and supports the importance of ASCT in patients of Myeloma and Lymphoma. We need more mature and longer follow up data to substantiate overall survival benefit in our cohort.

References:

1. *BARNES DW, CORP MJ, LOUTIT JF, NEAL FE. Treatment of murine leukaemia with X rays and homologous bone marrow; preliminary communication. Br Med J. 1956 Sep 15;2(4993):626-7. [PMC free article] [PubMed] [Reference list]*
2. *Multiple Myeloma: ESMO clinical practice guidelines- Ann Oncol 2013; 24 (Suppl 6):*
   Authors: P. Moreau, J. San Miguel, H. Ludwig, H. Schouten, M. Mohty, M. Dimopoulos, M. Dreyling
3. *The impact of ASCT on patients with newly diagnosed multiple myeloma who receive RVD induction: Marlise R. Luskin, Federico Campigotto, Paul G. Richardson, John Koreth, Irene M. Ghobrial, Robert L. Schlossman, Nikhil C. Munshi, Edwin P. Alyea, Robert J. Soiffer, Diane Warren, Muriel Gannon, Kathleen Finn, Kenneth C. Anderson, Edie A. Weller, Jacob P. Laubach*
4. *Have drug combinations supplanted stem cell transplantation in myeloma?*
   Antonio Palumbo1 and Federica Cavallo11Myeloma Unit, Division of Hematology, University of Torino, Torino, Italy
5. *Reversibility Of Renal Failure In Newly Diagnosed Multiple Myeloma Patients Treated With High Dose Dexamethasone-Containing Regimens And The Impact Of Novel Agents*
   Efstathios Kastritis, Athanasios Anagnostopoulos, Maria Roussou, Dimitra Gika, Charis Matsouka, Despina Barmparousi, Irini Gapsa, Erasmia Psimenou,Aristotle Bamias, MeletiosAthanasios Dimopoulos Haematologica April 2007 92: 546-549; Doi:10.3324/haematol.10759
6. *deLeval L, Hasserjian RP. Diffuse Large B-Cell Lymphomas and Burkitt Lymphoma. HematolOncolClin North Am. 2009;23:791–827. [PubMed]*
7. *High-dose chemotherapy and autologous stem cell transplantation for hodgkin's lymphoma in the kingdom of saudiarabia: king faisal specialist hospital and research center experience. Akhtar s1, abdelsalam m, elweshi a, al husseini h, janabii, rahal m, maghfoori.*

- x -

Modifications and Treatment Customizations during lockdown : A Guide

(Dept. Of Medical Oncology)

- Patients and caregivers undergo two successive screenings with thermal gun, once at the point of entry in the outpatient area and second at the point of entry to the department.
- Patient waiting area has been expanded to maintain social distancing norms.
- There is a separate donning and doffing corner for Personal Protective Equipment (PPE).
- Chemotherapy naïve patients are being screened routinely with RT-PCR for SARS COVID 2 virus before the start of treatment. They are subsequently tested only if they experience symptoms for coronavirus. Once a patient is tested positive for COVID, chemotherapy is temporarily stopped and later on resumed if repeat test results are negative. However hormonal treatments continue.
- Adequate distance is being maintained in the consultation area. Doctors and nurses are being provided a fresh set of gloves, face masks, face shields, gowns and goggles each day. Sanitizers are available in plenty. Nurses are administering drugs wearing PPE kits.
- Greater emphasis is given to chemotherapy administration on daycare basis. This includes patients with solid tumours as well as hematological malignancies. As per international guidelines – intensive long duration protocols mandating admission are being replaced with less intensive protocols without compromising efficacy.
- Use of biologics, immunotherapy and targeted therapy have certainly gone up. Recommendations from International bodies like ASCO, ESMO, ICON suggest – wider use of non-cytotoxic regimens during COVID 19 outbreak. Neo-adjuvant chemotherapy is being encouraged for surgical eligible patients to reduce long waiting periods.
- There has been liberal use of growth factors in order to reduce the frequency of hospital visits.
- Flexibility has been provided to patientsenabling them to carry out necessary investigations from validated laboratories. This facilitates a single day visit for consultation or treatment.
- A comprehensive guideline was created for the treating team to facilitate uninterrupted services during cyclone and lockdown in order to reduce visits and exposure. The Department has to its credit an article titled “Perception of Oncologists from developing nation during COVID 19 Pandemic”accepted for E-poster presentation at ESMO Asia Virtual Congress 2020.
- Additional helpline numbers were created for patients undergoing chemotherapy to resolve issues pertaining to chemotherapy in order to save time and prevent unnecessary travelling. Special appointment letters and transport passes are being provided to patients including one attendant to facilitate their travel during complete lockdown.
- Prior to admissions COVID testing is normally recommended. Admission without COVID RT- PCR test allowed only for emergency patients. They are initially kept in isolation and once tested negative for COVID 19, they are shifted to non – COVID ward.
- Common protocols and agents administered during lockdown : CAPOX, CAPIRI, GEMCAP, CAPTEM, Capecitabine monotherapy, Fulvestrant, Leuprolide, bisphosphonates, monoclonal antibodies, growth factors etc.
- Start of some lucrative patient assistance programs and support services through tie-ups and collaboration eg : Swathya Sathi.

ESMO ASIA 2020 CONGRESS, SINGAPORE (20-22 NOVEMBER 2020)

COVID ERA – PERCEPTION OF ONCOLOGISTS FROM A DEVELOPING NATION

Roy Rakesh [1], Prasad Snehangi [1], Gupta Ankita [1], Agarwala Vivek [2]

(Saroj Gupta Cancer Centre & Research Institute, Kolkata [1] ; Narayana Superspeciality Hospital, Howrah [2])

INTRODUCTION & BACKGROUND

During this global COVID-19 outbreak, all patients are facing problem in receiving treatment especially cancer patients. Cancer being a lethal disease, delay in treatment may be fatal. To manage the situation several international organizations have come up with very useful generalized guidelines for cancer management during COVID-19 pandemic. Still the availability of resources, infrastructure, state health policy, COVID incidence and approach of healthcare professionals differ. Cancer patients receiving systemic therapy are immunocompromised and the situation is further complicated by uncertainty of duration of this pandemic. This study aims to find out the perception and approaches of Indian oncologists – which might prove to be useful in nation specific delivery of cancer care during COVID Pandemic.

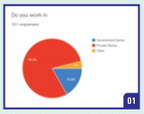
AIMS & OBJECTIVE

Perception of Indian Oncologists and their preferences and approaches to treatment during COVID pandemic.

METHODOLOGY

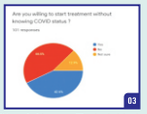
After taking consent, a Survey Form was circulated online amongst 101 oncologists (haemato / radiation / medical / surgical) across the country and responses collected.

RESULTS

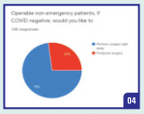


79.2% of the oncologists who participated in the survey practice in private sector, 16.8% of them in government sector and rest 4% other sectors.

50% oncologists were willing to postpone the investigations for the disease for stable patients and 50% were not.



42.6% oncologists were willing to start treatment without knowing the COVID status, while 44.6% were against the idea and 12.9% were indecisive.

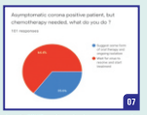


73% oncologists were willing to perform surgery right away considering the patients to be operable in nonemergency cases with a NEGATIVE COVID status and rest 27% postpone the surgery.

57% oncologists preferred concurrent CT-RT during COVID outbreak and 43% preferred sequential CT-RT.

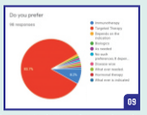
53.5% were comfortable prescribing chemotherapy via telemedicine and requesting patient to take the same at local place under trained physician. 46.5% were against the same.

RESULTS (CONTD...)



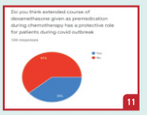
Asymptomatic COVID positive patients requiring chemotherapy - 64.4% oncologists were willing to wait for the virus to resolve and then start therapy and 35.6% were suggesting some form of oral medication and ongoing isolation.

89.1% preferred oral route of therapy over intravenous if there was an option in patients during COVID, rest 10.9 % preferred intravenous route.

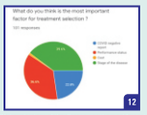


With respect to the type of cancer chemotherapy, 83.7% preferred targeted therapy, 8.2% preferred immunotherapy.

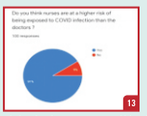
93.1 % preferred day care chemotherapy during COVID and 6.9% preferred inpatient chemotherapy.



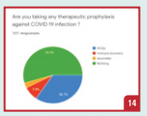
61% thought extended course of dexamethasone given as premedication during chemotherapy did not have a protective role for patients during COVID outbreak while rest 39 % thought it had a protective role.



39.6% thought stage of the disease was the most important factor, for 36.6 % it was the performance status of the patient, 22.8% it was the COVID status and for the remaining it was the cost.



91% oncologists thought nurses were at a higher risk of exposure to COVID infection than the doctors, and rest were against the same.



54.5% were not taking any prophylactic therapy against COVID-19 infection, 34.7% were taking prophylactic dose of HYDROXYCHLOROQUINE, 7.9 % were taking IMMUNOBOOSTERS and 2.9% taking AYURVEDIC medication.

DISCUSSION & CONCLUSION

Greater homogeneity in practice and alignment with International guidelines were noticed amongst oncologists of a developing nation during COVID outbreak. The above information might be useful in policy making.

Declaration : The author or co-authors have no conflict of interest whatsoever regarding the publication of this e-poster.

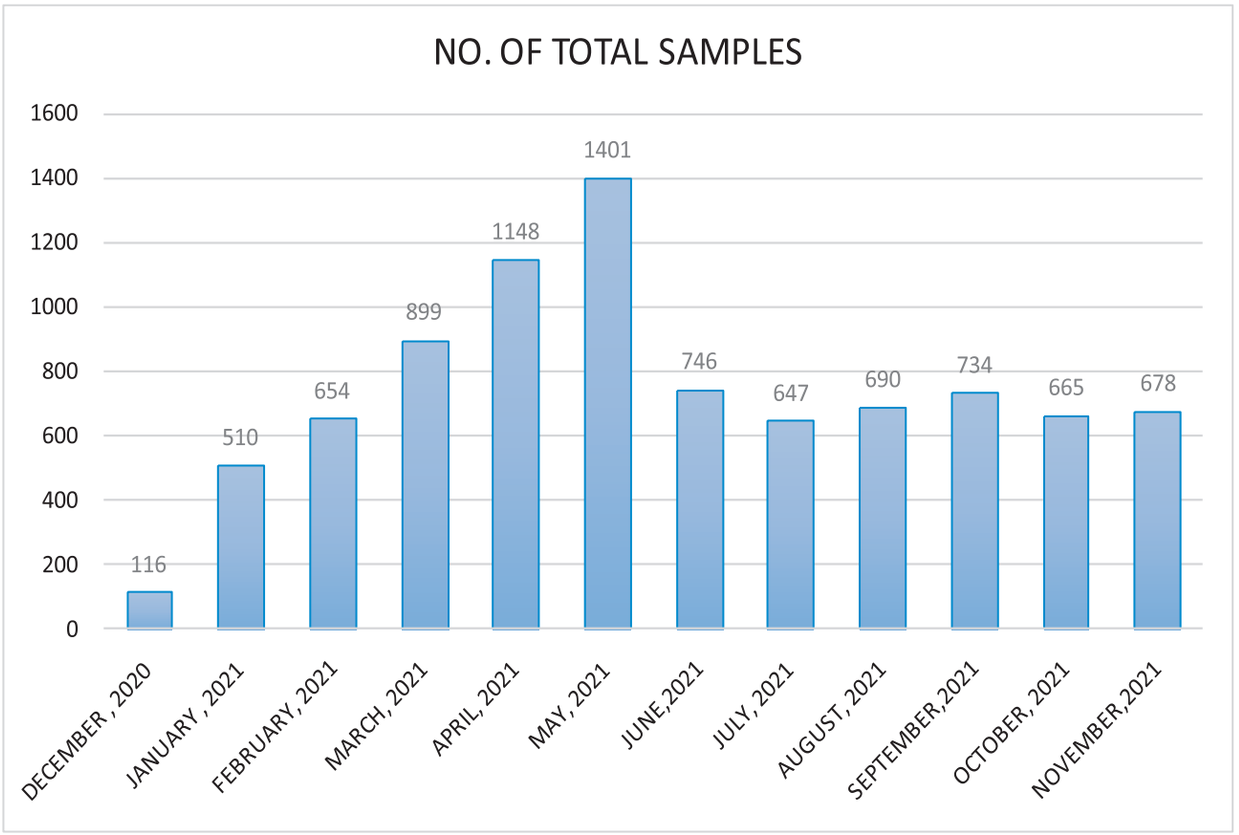
e-mail id (author) : rex4you@gmail.com

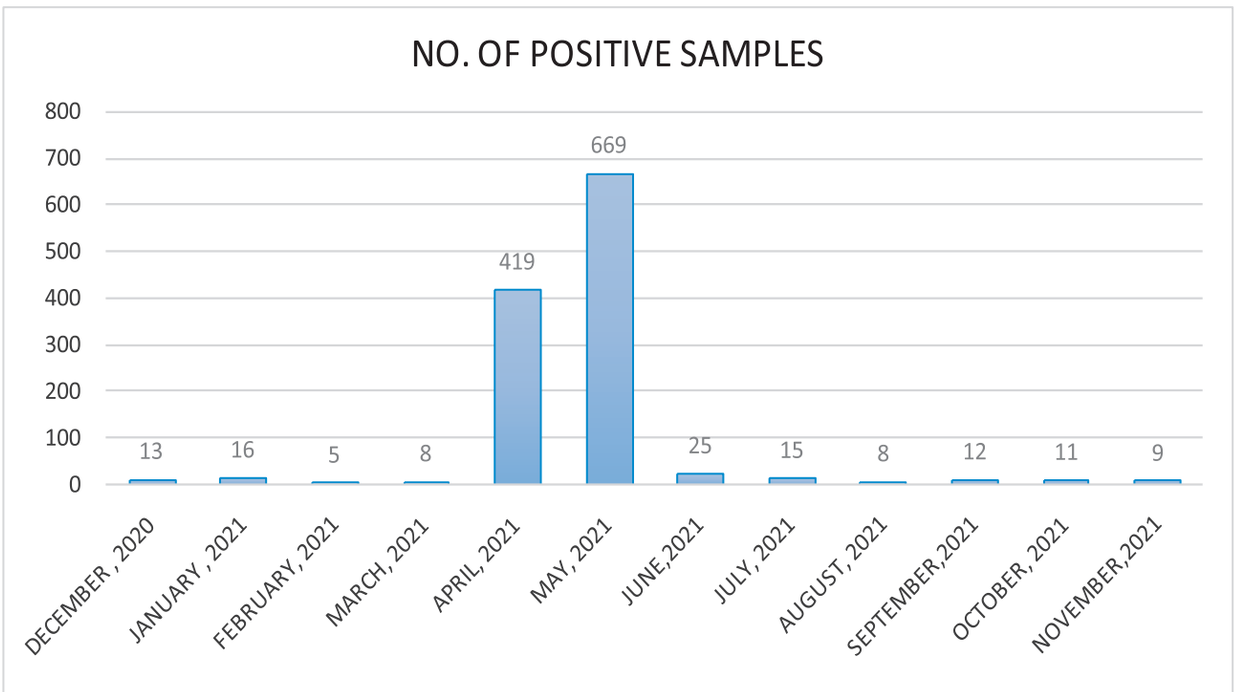
RT-PCR Based COVID-19 Detection at SGCCRI: A journey from the beginning till now

Authors: Ms. Koyel Banerjee (Laboratory Manager, Molecular Diagnostic Laboratory, SGCCRI); Dr. Somosree Ghosh (MD-Microbiologist, Molecular Diagnostic Laboratory, SGCCRI) & Dr. Somsubhra Nath (Scientist, Basic & Translational Research Division and Technical Director, Molecular Diagnostic Laboratory, SGCCRI)

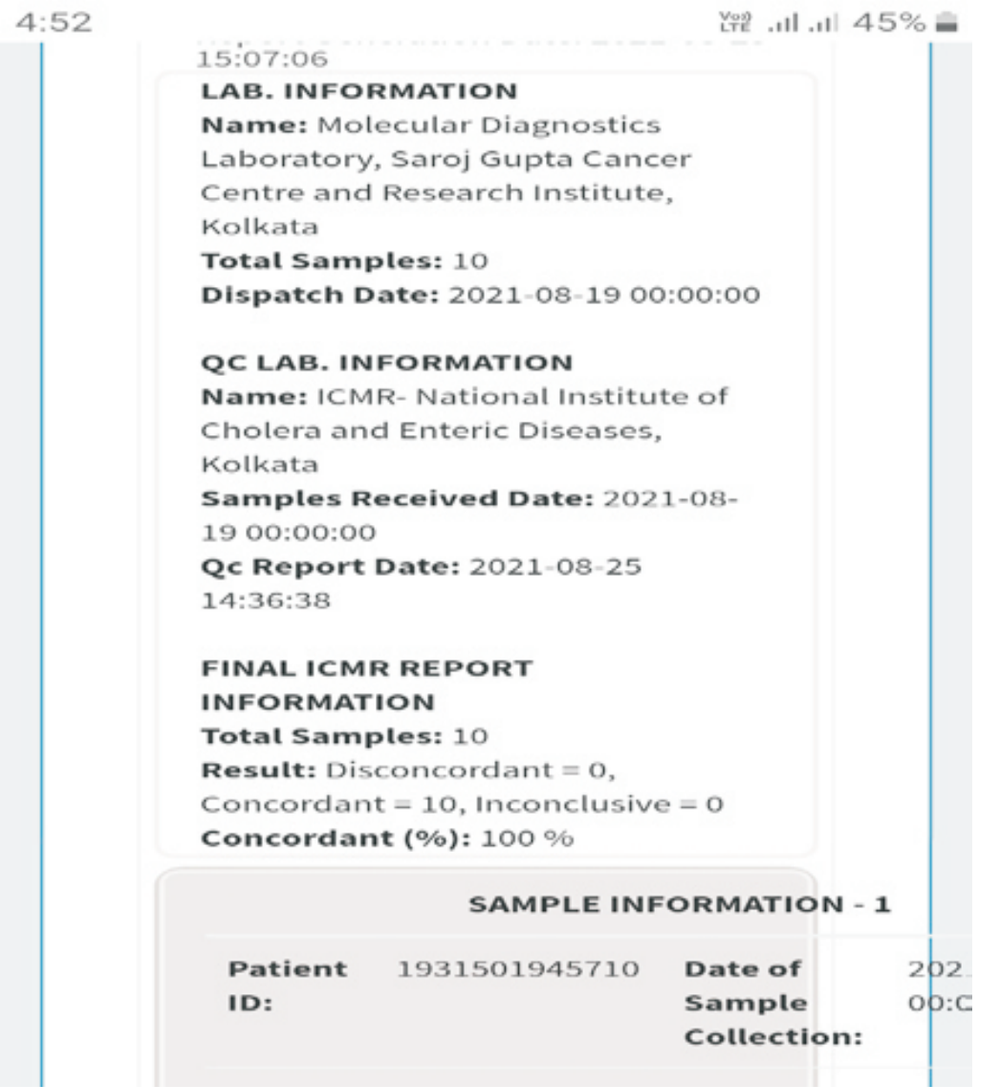
The global pandemic, COVID-19 infection has showed much of devastating effect on the man-kind. To cope up with the related adversitities and moreover, to go beyond this deadly obstacle, SGCCRI took up steps in various ways. First and foremost, SGCCRI has started its own RT-PCR laboratory for COVID-19 detection started from 22nd December, 2020. This system runs under the accreditation of NABL (received on 4th Dec, 2020) and approval from ICMR (received on 8th Dec, 2020). Indeed, this facility runs under the monitoring from Govt. of WB, Dept. of Health and Family Welfare (certified on 16th Dec, 2020). The quality control of the in-house testing is being assessed by Swasthya Bhavan, Govt. of WB, by cross-checking random samples in an interval of 15-30 days. Moreover, at the National level, the quality control is being monitored by ICMR at the bi-annual basis, for which NICED, Kolkata is acting as the state level nodal centre. Starting from 22nd December 2020, till 30th November this centre has conducted testing of 8888 samples, of which 1210 cases has been noted as positive for COVID-19 infection. The month-wise distribution of cases is provided in the figures.

MONTH (2020-2021)	NO. OF TOTAL SAMPLES	NO. OF POSITIVE SAMPLES
DECEMBER , 2020	116	13
JANUARY , 2021	510	16
FEBRUARY, 2021	654	5
MARCH, 2021	899	8
APRIL, 2021	1148	419
MAY, 2021	1401	669
JUNE,2021	746	25
JULY, 2021	647	15
AUGUST, 2021	690	8
SEPTEMBER,2021	734	12
OCTOBER, 2021	665	11
NOVEMBER,2021	678	9
TOTAL	**8888**	**1210**


NO. OF TOTAL SAMPLES
1600
1400
1200
1000
800
600
400
200
0
116
510
654
899
1148
1401
746
647
690
734
665
678
DECEMBER , 2020
JANUARY , 2021
FEBRUARY, 2021
MARCH, 2021
APRIL, 2021
MAY, 2021
JUNE,2021
JULY, 2021
AUGUST, 2021
SEPTEMBER,2021
OCTOBER, 2021
NOVEMBER,2021


NO. OF POSITIVE SAMPLES
800
700
600
500
400
300
200
100
0
13
16
5
8
419
669
25
15
8
12
11
9
DECEMBER , 2020
JANUARY , 2021
FEBRUARY, 2021
MARCH, 2021
APRIL, 2021
MAY, 2021
JUNE,2021
JULY, 2021
AUGUST, 2021
SEPTEMBER,2021
OCTOBER, 2021
NOVEMBER,2021

We humbly state that this centre has obtained 100% concordance in quality assurance by ICMR at National



level (as snapshot is added here).

We know there are more obstacles waiting in the coming days and we are determined to overcome those at our united best, from SGCCRI.

A study to find out if Polypharmacy is being practiced in Palliative Care patients in SGCCRI. Retrospective Study.

Dr Rakesh Roy, Dr Gautam Bhattacharjee, Dr Kuntal Ghosh,
Ms Sangeeta Das, MS Smritikana, Ms Anima,
(Dept. of Pain & Palliative Care)

BACKGROUND AND IDENTIFICATION OF THE PROBLEM

The World Health Organization (WHO) estimates that globally more than half of all medicines are prescribed inappropriately. Irrational use of medication is a major problem in India. Examples of this include; too many medicines per patient (polypharmacy), inappropriate use of antimicrobials and failure to prescribe in accordance with clinical guidelines4.

Polypharmacy is defined simply as the use of multiple medications by a patient. Patients with advanced cancer are especially at risk of polypharmacyreceiving multiple drugs to control symptoms, concomitant diseases as well as anti-cancer treatment1.Because of multiple systemic manifestations in advanced cancer, the medical team ends up giving several drugs resulting in polypharmacy. The general norm in Palliative care is – to limit admissions and encourage medications by the mouth, by the clock and by the ladder (WHO Analgesic Ladder). Admissions happen when the symptoms are difficult to address with medications and need parenteral treatment and interventions. Therefore the number of medications increase for inpatients compared to outpatients.

The risk of an adverse medication interaction is greater than 80%whenmore than seven medications are taken regularly2.Polypharmacy can lead to a prescribing cascade, poor adherence and is a risk factor for delirium.

PURPOSE OF THE STUDY

To identify the current trend in drug practice for admitted palliative care patients. To see whether polypharmacy is a routine practice or need based approach. This will help in identifying the adherence to Standard of Care and appropriate use of resources and create a template for future implementation. In order to do this following aims have been laid down -

AIMS

- To determine the degree of polypharmacy in advanced cancer patients.
- To determine the classes of medicines most commonly prescribed.
- To determine if analgesia is prescribed in accordance with the WHO analgesic ladder.
- To determine if patients know how many medications they are taking and the perceived benefit and harm of medications.

METHODHOLOGY

Study Subjects- 30 inpatients receiving only Palliative Care for terminal cancer at SGCCRI.

Study Nature &Duration– Retrospective, 4 months.

Data Source - The medical records (notes and medicine cards)of inpatients admitted in SGCCRI. The following were documented:

- Patient demographics
- Primary diagnosis
- Number of medications prescribed
- Dose & regime
- Category of drug (Analgesia, antiemetic, laxative, sedative, antipsychotic, nutritional supplement etc)

Exclusion Criteria:

- IV fluids,
- drugs not documented on the medicine card.
- Patients admitted in ICU or ITU receiving critical care.
- Post operative patients getting pain management
- Patients getting curative cancer treatment admitted for pain palliation.

- In addition to this a short patient questionnaire was conducted including ten questions. Data were collated and analyzed using excel.

RESULTS

The mean number of medications prescribed per patient was 11.7(range 3- 29). 77% of patients were taking >7 medications, 56% taking > 10 medications.

Commonest medication identified wereacid neutralizing drugs, most frequently a proton pump inhibitor. Analgesics were the second most commonly prescribed medication group followed by health supplements and antibiotics. 58% of patients were prescribed more than one health supplement, including multivitamin injections, glutamine and amino acids. Good number of patients were prescribed a benzodiazepineat night time for insomnia.

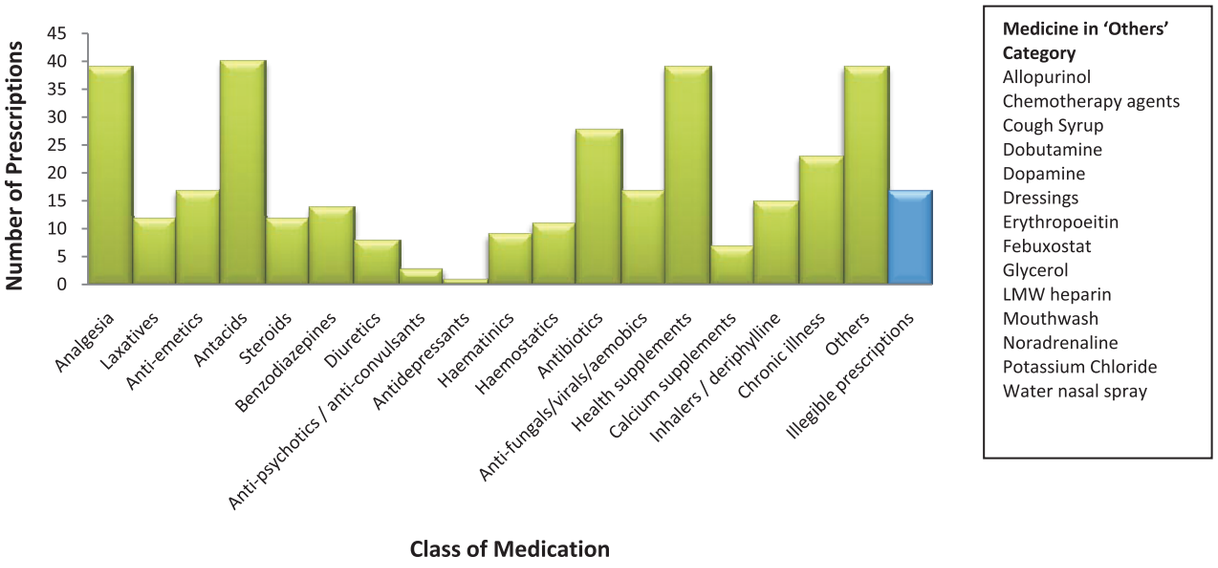


Chart 1: Frequency of prescriptions of each Class of Medication

Analgesics :70% of patients were prescribed analgesia, 73% in line with the WHO ladder. 60% were prescribed step three analgesia. Of those receiving morphine, only 35% were prescribed morphine for breakthrough pain and 3% were prescribed laxatives. 2% of the analgesic drugs prescribed were combination drugs (eg. Ultracet – paracetamol + tramadol).

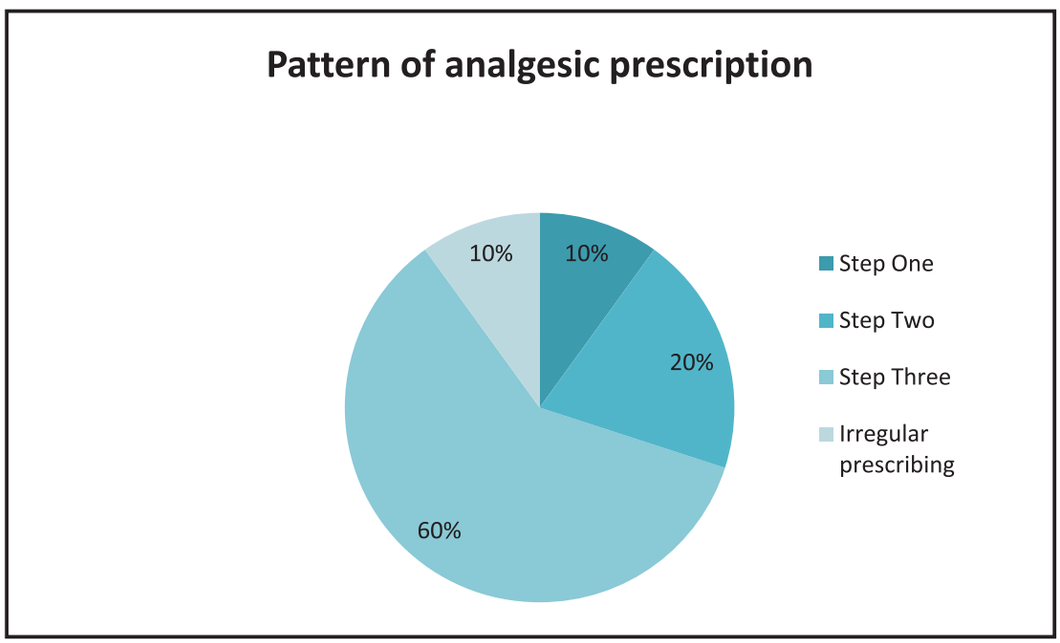
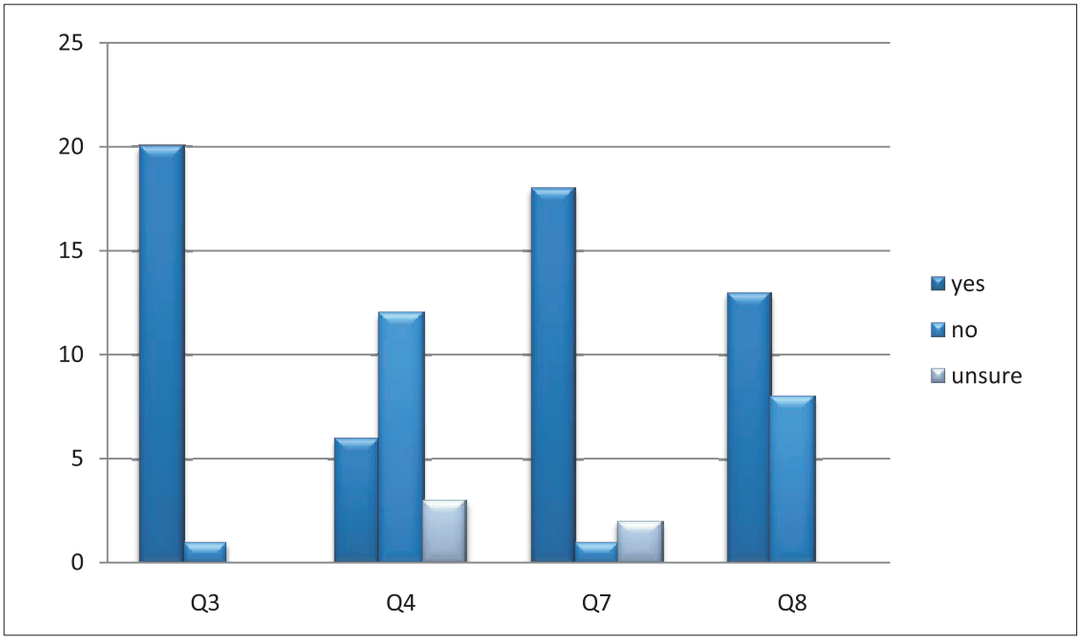


Chart2. Analgesia prescribing trend.

The dose and route of administration varied; the lowest dose prescribed forDexamethasone was 8mg per day and the highest 24mg. Prescriptions thatwere inappropriate for palliative care patients included dobutamine, noradrenaline, dopamine, erythropoietin, glycerol and glutamine.88% of medications were prescribed by brand name, 7% by generic name and 5% of prescriptions were illegible.

Patient Questionnaire

30% (9/30) of patients were unable to answer the questionnaires. Of the remaining 21 patients, 76% did not know how many drugs they were taking and 24% thought they were taking significantly less medicines than they were prescribed. Those that guessed underestimated by 29%-66%. No patients knew how many medications they were taking or over estimated the number.When asked if they knew what the medication was for 14% said they did, but when asked to in detail what they were no one was able to answer.
The graph below shows that, although 95% of those answering the questionnaire reported taking all their medication, 28% also said they have difficulty taking all their tablets. 86% said that they thought the medication made them feel better, although 62% would like to take less medication and a high number of patients reported adverse effects and side effects.



38% (8/21) of patients reported adverse reactions, and 29% (76/21) were unsure. 43% reported side effects, 24% (5/21) were unsure if they had experienced side effects.

DISCUSSION

This study demonstrates that the average number of medicines prescribed for palliative patients is 11.7 - substantially higher than in Europe where the average in the same population is 7.81.Over three-quarters of the patients were taking more than 7 medications, suggesting that polypharmacy is the norm rather than the exception. This puts patients at >80% risk of adverse drug interactions2.

Though 60% of patients were receiving strong opioids, approximately quarter of the patients did not receive analgesia in line with the WHO ladder, including prescriptions for breakthrough pain. The two patients who were prescribed the most medicines; 19 and 29 respectively had no analgesia prescribed. Studies show that 64%-85% of patients with advanced, metastatic or terminal cancer experience pain5,3. Analgesic prescription in this study was suboptimal.

88% of medications were prescribed by brand name. TheIndian market is flooded with over 70,000 formulations, compared to roughly350 preparations listed on the WHO Essential Drugs List6.Studies show that irrational prescribing is commonplace in India with high levels of polypharmacy and use of unnecessary medicines including a large number of vitamins and health tonics6,7, which is supported by this study.

This study is limited by the small number of patients included. It was beyond the scope of the study to assess patients' functional status and drug-drug interactions.

CONCLUSION

This study highlights the problem of polypharmacy and irrational prescribing in palliative cancer patients in India. There is a need for improved guidance, regulation and policies.

INTERVENTIONS / REMEDIAL MEASURES PLANNED

- To reduce the incidence of polypharmacy
- Incase patient is on polypharmacy – to restrict usage to bare essential life saving drugs
- To increase adherence of analgesic prescriptions to WHO Analgesic Ladder.
- To ensure that deserving candidates should not be deprived from STEP III Analgesia.

References:

1. *Kotlinska-Lemieszek A. et al., Polypharmacy in Patients With Advanced Cancer and Pain:A European Cross-Sectional Study of 2282 Patients. J Pain Symptom Manag 2014;48,6:1145–1159*
2. *Steinhauser KE et al. Factors considered important at the end of life by patients, family, physicians, and other care providers. JAMA 2000;284:2476–2482.*
3. *Twycross R, Harcourt J, Bergl S. A survey of pain in patients with advanced cancer. J Pain Symptom Manage 1996;12:273-82*
4. *Holloway K, Green T, Drug and Therapeutics Committees: A Practical Guide. Drug and Therapeutics Committees: A Practical Guide [accessed April2015.*
5. *Van den Beuken-van Everdingen M. H. J., de Rijke M. H. J., Kessels A. G.,Schouten H. C, van Kleef M. &Patijn J. Prevalence of pain in patients with cancer: a systematic review of the past 40 years Annals of Oncology 18: 1437–1449, 2007*
6. *Patel V, Vaidya R, Naik D, Borker P. Irrational drug use in India: A prescription survey from Goa. J Postgrad Med March 2005 Vol 51 (1):9-12.*
7. *Rambhade S, Shrivastava A, Rambhade A, Chakarborty A, Patil U. A survery on polypharmacy and use of inappropriate medications. Toxicology 2015;Vol 19-1:68-73*

---------- XXXXXX ----------

Journal scan: 2021

Dr Samir Bhattacharyya (Department of Surgical Oncology & Research)

As in previous issues of the scientific bulletin, the Editorial team presents some interesting publications in the field of oncology.

1. Izraely S, Witz IP. Site-specific metastasis: A cooperation between cancer cells and the metastatic microenvironment. Int. J. Cancer. 2021;148:1308–1322.

Abstract: The conclusion derived from the information provided in this review is that disseminating tumor cells (DTC) collaborate with the microenvironment of a future metastatic organ site in the establishment of organ-specific metastasis. We review the basic principles of site-specific metastasis and the contribution of the cross talk between DTC and the microenvironment of metastatic sites (metastatic microenvironment [MME]) to the establishment of the organ-specific premetastatic niche; the targeted migration of DTC to the endothelium of the future organ-specific metastasis;the transmigration of DTC to this site and the seeding and colonization of DTC in their future MME. We also discuss the role played by DTC-MME interactions on atumor dormancy and on the differential response of tumor cells residing in different MMEs to antitumor therapy. Finally, we summarize some studies dealing with the effects of the MME on a unique site-specific metastasis—brain metastasis.

Editorial Comment: Stephen Paget, with his “seed and soil” theory, first proposed the concept of site-specific metastasis. Since then, a lot of research effort has been put to understand the mechanisms of, and possible actionable targets for, site-specific metastasis. The major areas include defining the molecular signature of cancer cells that enable their establishment as metastatic lesions in different organs; the molecular signature of the host microenvironmental cells supporting or inhibiting this establishment; the modus operandi by which such molecules exert their pro- or anti-metastasis functions; the functional significance of interactions between metastasizing cancer cells with cells residing in or recruited to the microenvironment of specific organ sites and the impact of site-specific metastasis on and response to therapy. This review discusses recent developments in the establishment of site-specific metastasis and organ specificity, and should be relevant to researchers, and clinicians as well.

2. Oudkerk M, Liu SY, Heuvelmans MA, Walter JE, Field JK. Lung cancer LDCT screening and mortality reduction — evidence, pitfalls and future perspectives. Nature Rev Clin Oncol 2021;18:135–151.

Abstract: In the past decade, the introduction of molecularly targeted agents and immune-checkpoint inhibitors has led to improved survival outcomes for patients with advanced-stagelung cancer; however, this disease remains the leading cause of cancer-related mortality worldwide. Two large randomized controlled trials of low-dose CT (LDCT)-based lung cancerscreening in high-risk populations — the US National Lung Screening Trial (NLST) and NELSON —have provided evidence of a statistically significant mortality reduction in patients. LDCT-based screening programmes for individuals at a high risk of lung cancer have already been implemented in the USA. Furthermore, implementation programmes are currently underway in the UK followingthe success of the UK Lung Cancer Screening (UKLS) trial, which included the Liverpool HealthLung Project, Manchester Lung Health Check, the Lung Screen Uptake Trial, the West London LungCancer Screening pilot and the Yorkshire Lung Screening trial. In this Review, we focus on the current evidence on LDCT-based lung cancer screening and discuss the clinical developments.

Editorial Comments: Lung cancer is currently both the most commonly diagnosed cancer (11.6% of all cancer diagnoses) and the leading cause of cancer-related mortality (18.4%) in both men and women worldwide. Recent introduction of molecularly targeted agents and immune-checkpoint in hibitors has led to improved survival outcomes in advanced stage lung

cancer. However, these agents are beneficial only for a limited subset of patients, and the majority of advanced lung cancer patients succumb to their disease. On the other hand, patients with early-stage lung cancer, if treated properly, have a much better prognosis. Hence, the main strategy aimed at substantially reducing lung cancer mortality has been two-pronged; viz. prevention and early detection. Early detection using low-dose CT (LDCT)-based screening in asymptomatic

individuals can detect lung cancer at an early stage, and can be effectively treated. This review discusses evidences regarding different options in varying groups of population, their efficacy, and cost effectiveness. This informative article will be helpful for those dealing with this dreaded disease.

3. Bahadoer RP, Dijkstra EA, van Etten B, Marijnen CAM, Putter H, Kranenbarg EMK, et al and the RAPIDO collaborative investigators. Short-course radiotherapy followed by chemotherapy before total mesorectal excision (TME) versus preoperative chemoradiotherapy, TME, and optional adjuvant chemotherapy in locally advanced rectal cancer (RAPIDO): a randomised, open-label, phase 3 trial. Lancet Oncol 2021; 22: 29–42.

Summary:
Background: Systemic relapses remain a major problem in locally advanced rectal cancer. Using short-course radiotherapy followed by chemotherapy and delayed surgery, the Rectal cancer And Preoperative Induction therapy followed by Dedicated Operation (RAPIDO) trial aimed to reduce distant metastases without compromising locoregional control.
Methods: In this multicentre, open-label, randomised, controlled, phase 3 trial, participants were recruited from 54 centres in the Netherlands, Sweden, Spain, Slovenia, Denmark, Norway, and the USA. Patients were eligible if they were aged 18 years or older, with an Eastern Cooperative Oncology Group (ECOG) performance status of 0–1, had abiopsy-proven, newly diagnosed, primary, locally advanced rectal adenocarcinoma,which was classified as high risk on pelvic MRI (with at least one of the following criteria: clinical tumour [cT] stage cT4a or cT4b, extramural vascular invasion, clinical nodal [cN] stage cN2, involved mesorectal fascia, or enlarged lateral lymph nodes), were mentally and physically fit for chemotherapy, and could be assessed for staging within 5 weeks before randomisation. Eligible participants were randomly assigned (1:1), using a management system with a randomly varying block design (each block size randomly chosen to contain two to four allocations), stratified by centre, ECOG performance status, cT stage, and cN stage, to either the experimental or standard of care group. All investigators remained masked for the primaryendpoint until a prespecified number of events was reached. Patients allocated to the experimental treatment group received short-course radiotherapy (5 × 5 Gy over a maximum of 8 days) followed by six cycles of CAPOX chemotherapy (capecitabine 1000 mg/m² orally twice daily on days 1–14, oxaliplatin 130 mg/m² intravenously on day 1, and a chemotherapy-free interval between days 15–21) or nine cycles of FOLFOX4 (oxaliplatin 85 mg/m² intravenously on day 1, leucovorin [folinic acid] 200 mg/m² intravenously on days 1 and 2, followed by bolus fluorouracil 400 mg/m²intravenously and fluorouracil 600 mg/m² intravenously for 22 h on days 1 and 2, and a chemotherapy-free interval between days 3–14) followed by total mesorectal excision. Choice of CAPOX or FOLFOX4 was per physician

discretion or hospital policy. Patients allocated to the standard of care group received 28 daily fractions of 1•8 Gy up to 50•4 Gy or 25 fractions of 2•0 Gy up to 50•0 Gy (per physician discretion or hospital policy), with concomitant twice-daily oral capecitabine 825 mg/m² followed by total mesorectal excision and, if stipulated by hospital policy, adjuvant chemotherapy with eight cycles of CAPOX or 12 cycles of FOLFOX4. The primary endpoint was 3-year disease-related treatment failure, defined as the first occurrence of locoregional failure, distant metastasis, new primary colorectal tumour, or treatment-related death, assessed in the intention-to-treat population. Safety was assessed by intention to treat. This study is registered with the EudraCT, 2010-023957-12, and Clinical Trials. gov, NCT01558921, and is now complete.

Findings: Between June 21, 2011, and June 2, 2016, 920 patients were enrolled and randomly assigned to a treatment, of whom 912 were eligible (462 in the experimental group; 450 in the standard of care group). Median follow-up was 4•6 years (IQR 3•5–5•5). At 3 years after randomisation, the cumulative probability of disease-related treatment failure was 23•7% (95% CI 19•8–27•6) in the experimental group versus 30•4% (26•1–34•6) in the standard of care group(hazard ratio 0•75, 95% CI 0•60–0•95; p=0•019). The most common grade 3 or higher adverse event during preoperative therapy in both groups was diarrhoea (81 [18%] of 460 patients in the experimental group and 41 [9%] of441 in the standard of care group) and neurological toxicity during adjuvant chemotherapy in the standard of caregroup (16 [9%] of 187 patients). Serious adverse events occurred in 177 (38%) of 460 participants in the experimental group and, in the standard of care group, in 87 (34%) of 254 patients without adjuvant chemotherapy and in 64 (34%) of187 with adjuvant chemotherapy. Treatment-related deaths occurred in four participants in the experimental group (one cardiac arrest, one pulmonary embolism, two infectious complications) and in four participants in the standard ofcare group (one pulmonary embolism, one neutropenic sepsis, one aspiration, one suicide due to severe depression).

Interpretation: The observed decreased probability of disease-related treatment failure in the experimental group is probably indicative of the increased efficacy of preoperative chemotherapy as opposed to adjuvant chemotherapy inthis setting. Therefore, the experimental treatment can be considered as a new standard of care in high-risk locallyadvanced rectal cancer.
Editorial Comments: along with the next.

4. Conroy T, Lamfichekh N, Etienne P, Rio E, Francois E, Mesgouez-Nebout N, et al.on behalf of the Unicancer Gastrointestinal Group and Partenariat de Recherche enOncologie Digestive (PRODIGE) Group. Total neoadjuvant therapy with mFOLFIRINOX versus preoperative chemoradiation in patients with locally advanced rectal cancer: final results of PRODIGE 23 phase III trial, a UNICANCER GI trial. Lancet Oncol 2021; 22: 702–15.

Summary
Background: Treatment of locally advanced rectal cancer with chemoradiotherapy, surgery, and adjuvant chemotherapy controls local disease, but distant metastases remain common. We aimed to assess whether administering neoadjuvantchemotherapy before preoperative chemoradiotherapy could reduce the risk of distant recurrences.

Methods: We did a phase 3, open-label, multicentre, randomised trial at 35 hospitals in France. Eligible patients were adults aged 18–75 years and had newly diagnosed, biopsy-proven, rectal adenocarcinoma staged cT3 or cT4 M0, with a WHO performance status of 0–1. Patients were randomly assigned (1:1) to either the neoadjuvant chemotherapy group or standard-of-care group, using an independent web-based system by minimisation method stratified by centre, extramural extension of the tumour into perirectal fat according to MRI, tumour location, and stage. Investigators and participants were not masked to treatment allocation. The neoadjuvant chemotherapy group received neoadjuvant chemotherapy with FOLFIRINOX (oxaliplatin 85 mg/m², irinotecan 180 mg/m², leucovorin400 mg/m², and fluorouracil 2400 mg/m² intravenously every 14 days for 6 cycles), chemoradiotherapy (50 Gy during 5 weeks and 800 mg/m² concurrent oral capecitabine twice daily for 5 days per week), total mesorectal excision, and adjuvant chemotherapy (3 months of modified FOLFOX6 [intravenous oxaliplatin 85 mg/m² and leucovorin400 mg/m², followed by intravenous 400 mg/m² fluorouracil bolus and then continuous infusion at a dose of2400 mg/m² over 46 h every 14 days for six cycles] or capecitabine [1250 mg/m² orally twice daily on days1–14 every 21 days]). The standard-of-care group received chemoradiotherapy, total mesorectal excision, and adjuvantchemotherapy (for 6 months). The primary endpoint was disease-free survival assessed in the intention-to-treatpopulation at 3 years. Safety analyses were done on treated patients. This trial was registered with EudraCT (2011-004406-25) and ClinicalTrials.gov (NCT01804790) and is now complete.

Findings: Between June 5, 2012, and June 26, 2017, 461 patients were randomly assigned to either the neoadjuvant chemotherapy group (n=231) or the standard-of-care group (n=230). At a median follow-up of 46•5 months(IQR 35•4–61•6), 3-year disease-free survival rates were 76% (95% CI 69–81) in the neoadjuvant chemotherapy group and 69% (62–74) in the standard-of-care group (stratified hazard ratio 0•69, 95% CI 0•49–0•97; p=0•034). Duringneoadjuvant chemotherapy, the most common grade 3–4 adverse events were neutropenia (38 [17%] of 225 patients) and diarrhoea (25 [11%] of 226). During chemoradiotherapy, the most common grade 3–4 adverse event was lymphopenia (59 [28%] of 212 in the neoadjuvant chemotherapy group vs 67 [30%] of 226 patients in the standard-of-caregroup). During adjuvant chemotherapy, the most common grade 3–4 adverse events were lymphopenia (18 [11%]of 161 in the neoadjuvant chemotherapy group vs 42 [27%] of 155 in the standard-of-care group), neutropenia (nine [6%] of 161 vs 28 [18%] of 155), and peripheral sensory neuropathy (19 [12%] of 162 vs 32 [21%] of 155). Serious adverse events occurred in 63 (27%) of 231 participants in the neoadjuvant chemotherapy group and 50 (22%) of 230 patients in the standard-of-care group (p=0•167), during the whole treatment period. During adjuvant therapy, serious adverse events occurred in 18 (11%) of 163 participants in the neoadjuvant chemotherapy group and 36 (23%) of 158 patients in the standard-of-care group (p=0•0049). Treatment-related deaths occurred in one (<1%) of 226 patients in the neoadjuvant chemotherapy group (sudden death) and two (1%) of 227 patients in the standard-of-care group (one sudden death and one myocardial infarction).

Interpretation: Intensification of chemotherapy using FOLFIRINOX before preoperative chemoradiotherapy significantly improved outcomes compared with preoperative chemoradiotherapy in patients with cT3 or cT4 M0 rectal cancer. The significantly improved disease-free survival in the neoadjuvant chemotherapy group and thedecreased neurotoxicity

indicates that the perioperative approach is more efficient and better tolerated than adjuvantchemotherapy. Therefore, the PRODIGE 23 results might change clinical practice.
Editorial Comments: For last few decades, neoadjuvantlong-course chemoradiotherapy (LC-CRT) or short-course radiotherapy (SCRT) has been widely accepted as standard of care stage II-III rectal cancer. However, several concerns remain. Firstly, a significant number of patients still develop disease failure. Secondly, postoperative adjuvant chemotherapy, though often administered, has not been shown to improve outcome. Thirdly, increasing radiotherapy-to-surgery interval has been shown to improve tumor regression. This opens up a window of opportunity to deliver

sequential, preoperative chemotherapy. Finally, incorporation of systemic chemotherapy into the neoadjuvant protocol increases the proportion of patients achieving complete clinical response, potentially bettering the probability of a wait-and-watch approach. The two afore-mentioned well-designed randomized controlled trials have reported on the outcome of a new paradigm in the treatment of locally advanced rectal cancer and have the potential of changing the practice pattern. The two trials have certain similarities, and differences. Both were run by prestigious collaborative groups, and compared the efficacy of additional preoperative chemotherapy to standard LC-CRT or SCRT. There were important differences also.

Fig 1. Study design of RAPIDO and PRODEGE 23 trials.

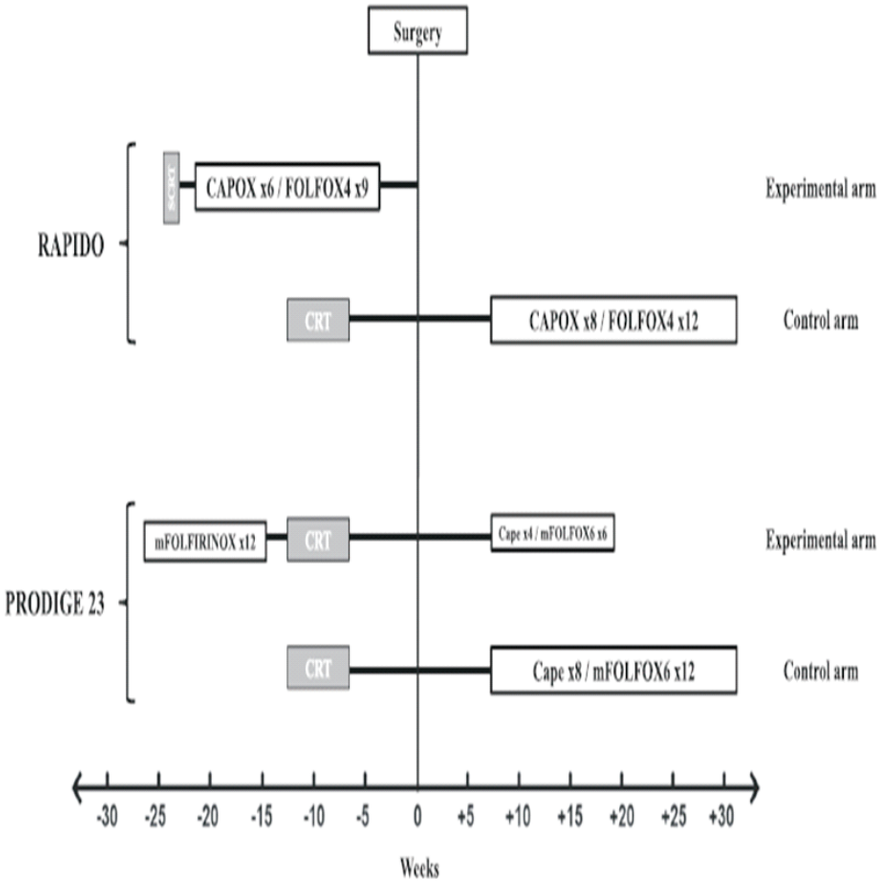


Table 1. Efficacy data from RAPIDO and PRODEGE 23 trials.

	RAPIDO	PRODEGE 23
Primary endpoint	Disease related treatment failure (DRTF) 30.4% (vs 23.7%) HR 0.75, p = 0.019	Disease free survival (DFS) 75.5% (vs 68.5%) HR 0.69, p = 0.034
pCR rate	28.4% (vs 14.3%) OR 2.37, p < 0.0001	27.8% (vs 12.1%) p < 0.001
Locoregional failure (at 3 years)	8.3% (vs 6.0%) HR 1.42, p = 0.12	Not reported
Distant metastases (at 3 years)	(Cumulative probability) 20.0% (vs 26.8%) HR 0.69, p = 0.0048	(Metastasis-free survival) 78.8% (vs 71.7%) HR 0.64, p = 0.017
OS (at 3 years)	89.1% (vs 88.8%) HR 0.92, p = 0.59	90.8% (vs 87.7%) HR 0.65, p = 0.07

The data presented in these two trials, though preliminary, appear robust and compelling in justifying routine adoption of TNT in clinical practice. However, statistically significant improvements in overall survival (OS) were not noted in experimental arms in either of the trials. DFS and (even less) DRTF are notvalidated surrogates for OS in rectal cancer. Even with these limitations, the two trials together openup a new pathway in management of locally rectal cancer, especially as improvements in DFS and DRTF were achieved mostly due to better distant tumor control, a problem long faced by the oncology community.

5. Park SH, Lim DH, Sohn TS, Lee J, Zang DY, Kim ST et al for the ARTIST 2 investigators. A randomized phase III trial comparing adjuvant single-agent S1, S-1 with oxaliplatin, and postoperative chemoradiation with S-1 and oxaliplatin in patients with node-positive gastric cancer after D2 resection: the ARTIST 2 trial. Ann Oncol 2021;32(3):368-374. Background: Adjuvant chemotherapy and chemoradiotherapy are some of the standards of care for gastric cancer (GC).

The Adjuvant chemoRadioTherapy In Stomach Tumors (ARTIST) 2 trial compares two adjuvant chemotherapy regimens and chemoradiotherapy in patients with D2-resected, stage II or III, node-positive GC.

Patients and methods: The ARTIST 2 compared, in a 1:1:1 ratio, three adjuvant regimens: oral S-1 (40-60 mg twice daily 4 weeks on/2 weeks off) for 1 year, S-1 (2 weeks on/1 week off) plus oxaliplatin 130 mg/m2 every 3 weeks (SOX) for 6 months, and SOX plus chemoradiotherapy 45 Gy (SOXRT). Randomization was stratified according to surgery type (total or subtotal gastrectomy), pathologic stage (II or III), and Lauren histologic classification (diffuse or intestinal/ mixed). The primary endpoint was disease-free survival (DFS) at 3 years; a reduction of 33% in the hazard ratio (HR) for DFS with SOX or SOXRT, when compared with S-1, was considered clinically meaningful. The trial is registered at clinicaltrials.gov (NCT0176146).

Results: A total of 546 patients were recruited between February 2013 and January 2018 with 182, 181, and 183 patientsin the S-1, SOX, and SOXRT arms, respectively. Median follow-up period was 47 months, with 178 DFS events observed. Estimated 3-year DFS rates were 64.8%, 74.3%, and 72.8% in the S-1, SOX, and SOXRT arms, respectively. HR for DFS inthe control arm (S-1) was shorter than that in the SOX and SOXRT arms: S-1 versus SOX, 0.692 (P ¼ 0.042) and S-1 versusSOXRT, 0.724 (P ¼ 0.074). No difference in DFS was found between SOX and SOXRT (HR 0.971; P ¼ 0.879). Adverse events were as anticipated in each arm, and were generally well-tolerated and manageable.

Conclusions: In patients with curatively D2-resected, stage II/III, node-positive GC, adjuvant SOX or SOXRT was effectivein prolonging DFS, when compared with S-1 monotherapy. The addition of radiotherapy to SOX did not significantly reduce the rate of recurrence after D2 gastrectomy.

Editorial Comments: The practice of adjuvant Chemoradiotherapy (CRT) in gastric cancer is based on the US Intergroup(INT)-0116 trial, that showed significant improvement in over-all survival after postoperative CRT as compared to surgery alone (40% versus 28% at 5 years) This trial was criticized for poor quality of surgery (only 10% of all patients had an adequatelymph node dissection).It has been suggested that adjuvant CRT compensated for poor loco-regional control resulting from inadequate surgery. However, NCCN guidelines still continue to recommend adjuvant CRT in locally advanced gastric cancer, albeit with a category of only level 2B. The issue has been investigated in Europe as well as in the East. The CRITICS trial in Europe and the ARTIST 1 and 2 trials from Korea reached similar conclusion, viz. adjuvant CRT does not have any significant benefit in gastric cancer patients treated with perioperative chemotherapy and surgery. The specific question addressed by the ARTIST 2

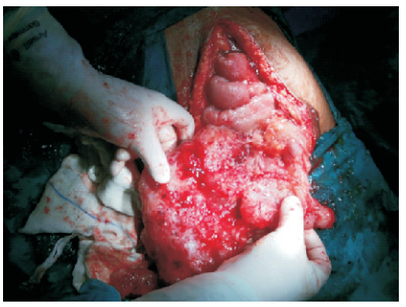
Trial was whether adjuvant CRT had any benefit in node-positive gastric cancer, as suggested after a subset analysis from ARTIST 1 trial. It was conclusively shown, that adjuvant CRT had no additional benefit over chemotherapy alone in node-positive gastric cancer. Thus, adjuvant CRT has probably reached the end of the road in the management scenario of locally advanced gastric cancer. However, radiotherapy may still have a place in the multimodality management of gastric cancer. The Preoperative Therapy for Gastric and Esophagogastric Junction Adenocarcinoma (TOPGEAR), a phase III Trial of patients with resectable gastric cancer to compare neoadjuvant chemotherapy with nCRT is currently underway. Neoadjuvant CRT has several theoretical advantages, such as, enhancing tumor sensitivity to chemotherapy and improving adherence rates prior to surgical treatment. So, possibly, the time to toll the bell on the role of radiotherapy in gastric cancer has no come yet, and more research is warranted.

-- x--

Pic Ur Quiz

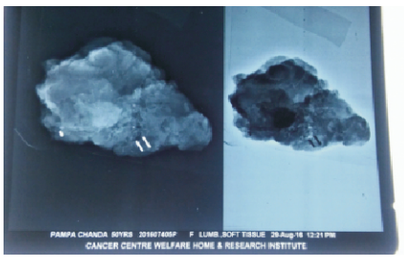
Dr. Arnab Gupta
(Department of Surgical Oncology & Research)

Qs 1. a)What is the diagnosis? b)What is the treatment?



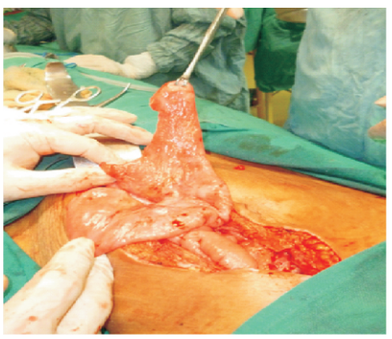
Ans 1. a)Pseudomyxoma peritonei. b)Cytoreductive surgery with HIPEC.

Qs 2. What is being done during a Breast Conservation surgery and why?



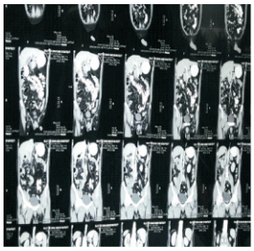
Ans 2. Specimen Mammography. This is to ensure that the radiological abnormality has been excised with clear margins. The radio-opaque clips are used for the orientation of the specimen. There may be complete resolution of the breast tumour after Neo-adjuvant chemotherapy and it is important in such cases to ensure that the radio-opaque marker which was placed at the centre of the tumour before chemotherapy has been taken out. Also, indicated for impalpable lesions esp. D

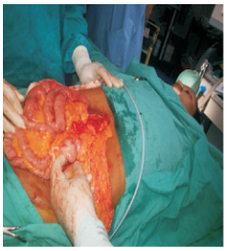
Qs 3. a) Describe the abnormalities. b)What would be the treatment?



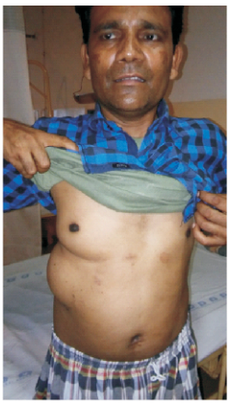
Ans 3. a)Meckel's Diverticulum with Intrinsic tumour at the tip, most likely Adenocarcinoma arising from the extrinsic Gastric mucosa. b)Surgical resection of the portion of the intestine with draining nodes with/ without adjuvant chemotherapy depending upon the stage.

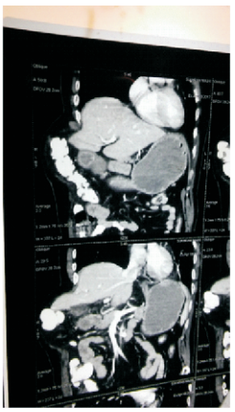
Qs 4. a) What anomaly has this patient got? b) What age group do they normally present and how?





Ans 4. a) Malrotation of gut with Caecum lying in the left Iliac fossa b) Malrotation of gut is a rare entity and mostly presents in the 1st month of life for obstructive symptoms from Ladd's band. Presentation in adulthood is seen in only 10- 15% cases as incidental finding or at autopsy.

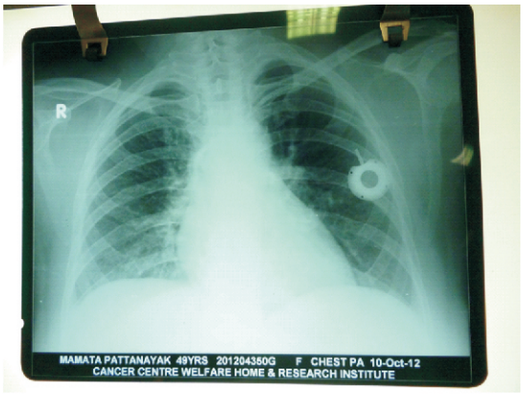




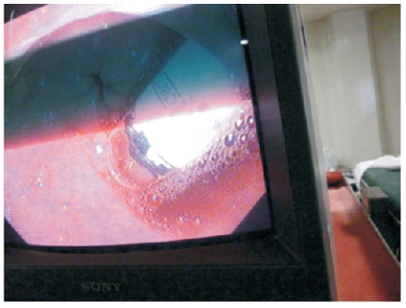
Qs 5. a) What congenital anomaly has this patient with Ca- Gallbladder got? b) What modification of the Incision would be required for him?

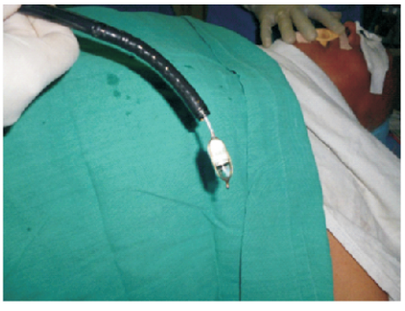
Ans 5. a) Partial congenital agenesis of the right lower chest wall with herniation of right lobe of liver and colon. b) Hockey stick/ Mid line incision

Qs 6. a) What is the diagnosis? b) How would you manage?



Ans 6 a) Migration of catheter into the right atrium and ventricle after detachment from the Chemoport. b) Retrieval by snare with the help of Interventional Radiology.





Qs 7. a) The patient was being investigated for repeated vomiting and weight loss. What has been found on Endoscopy?

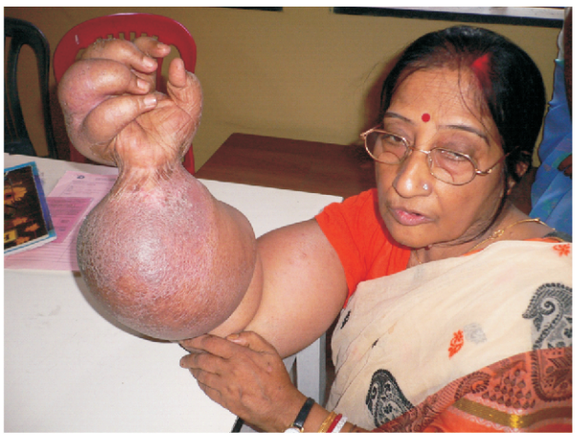
Ans 7 a) Gastric outlet obstruction with a Capsule Enoscope being stuck there which was retrieved by a Dormia basket.

Qs 8. What procedures has this patient undergone & possible diagnosis?

Ans 8. Tracheostomy and PEG (Percutaneous Endoscopic Gastrostomy). CVA/ Brain Tumour with patent Upper GI tract for which PEG was possible.

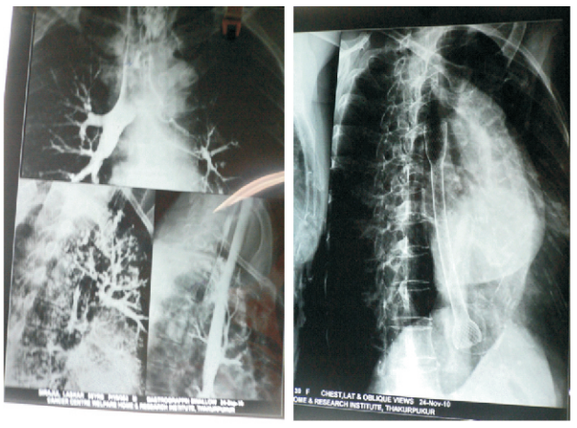
Qs 9. a) What rare complication has this patient developed after being previously treated for Ca- Breast?

b) What would be the treatment?



Ans 9. a) Angiosarcoma arising from chronic lymphoedema after Surgery and radiotherapy for locally advanced Ca- Breast b) Hind quarter amputation

Qs 10 What is the diagnosis and what has been done on a middle aged patient who presented with progressive dysphagia and later on coughing on food intake.



Ans 10 Barium swallow showing spillage of dye into the airways suggesting Tracheo-osophageal fistula in a case of Ca- Mid 1/3 Oesophagus. Self Expansile covered metal stent has been deployed.

Qs 11. Describe the abnormalities and the possible diagnosis

Ans 11. Multiple Neurofibromatosis, a large protuberant growth over the right gluteal region with skin ulceration, and a scar adjacent to it. Sarcomatous change in Neurofibromata which has recurred after previous surgery.

Qs 12 a) What procedure has been done on this patient? b) What are the other modalities?

Ans 12 a) Breast conservation Surgery with Sentinel Node Biopsy with Indo Cyanine Green. Looking at the Axillary Incision possible complete ALND was done. b) Radio Isotope, Blue dye alone or in combination.

WEEKLY CME (2020- 2021)

02/01/2020	• Small Cell Lung Cancer : What is New.	Speaker : Dr. Rakesh Roy (MEDICAL ONCOLOGY)
09/01/2020	• Can Assist Breast, Prognostication for early stage Breast Cancer.	Speaker : Ms. Sukriti Malpani (Product Manager, Oncostem Diagnostics Pvt Ltd)
16/01/2020	• Drug induced Liver Injury .	Speaker : Dr. Subrata Paul
23/01/2020	• Management of Non Small Cell Lung Cancer.	Speaker : Dr. Himanshu Pruthi (RADIOTHERAPY)
30/01/2020	• Prevention & Prophylaxis of infectionin the Haematology Work.	Speaker : Dr. Tusti Ganguly (HEMATO ONCOLOGY)
06/02/2020	• Ca-Cervix, latest Staging & Management.	Speaker : Dr. Himanshu Pruthi (RADIOTHERAPY)
13/02/2020	• Alpha Radiotherapy	Speaker: Dr. A. David Perianayagam (PHYSICIST)
20/02/2020	• i) Updates in Renal Cell Ca ii) Ca- Liver	Speaker : Dr. Rakesh Roy (RADIOTHERAPY) Speaker :Dr. Kabir Mody (Consultant Medical Oncologist, Mayo Clinic, USA)
27/02/2020	• Recent updates & treatment approaches for the management of advanced Renal Cell Ca.	Speaker : Dr. Bivas Biswas (Consultant Medical Oncologist, Tata Medical Centre, Kolkata)
05/03/2020	• Her2Neu Positive Breast Cancer- Where are we heading.	Speaker : Dr. Rakesh Roy (RADIOTHERAPY)
12/03/2020	• Recent Updates & Line of Therapy for the management of Metastatic Renal Cell Ca .	Speaker : Dr. Deepak Dabkara (Consultant Medical Oncologist, Tata Medical Centre, Kolkata)
12/11/2020	• Role of TPN in Chemotherapy Patients.	Speaker : Dr. Sudip Halder (SURGERY)
19/11/2020	• Code Blue Analysis & Update. • Discussion On Medical Records & Audit. • NABH Update	Speaker : Dr. Subhamoy Pal Dr.Amit Mukhopadhyay Mrs. Rita Das
26/11/2020	• Onco risk in assisted reproductive technology.	Speaker: Dr. Biman Chakraborty (GYNAECOLOGY)

03/12/2020	• NABH- : Understanding PSQ (Patient Safety Quotients)	Speaker : Mrs. Abanti Gopan (Principal Assessor & Faculty for NABH,)
10/12/2020	• Bliss of Paediatric Surgeon, a philosophical Idea.	Speaker : Dr. Amal Chakraborty (PEDIATRIC SURGERY)
17/12/2020	• Sentinel nodes in Cervical and Endometrial Ca- Procedure & rationale: Why do we need clinical trials. • SENTICOL 3 study – GCIG KolGo TRg Collaboration. • Pathology corner discussion on technique and pros & cons .	Speaker : Dr. Asima Mukhopadhyay (Director, Kolgo TRG)
24/12/2020	• Ca- Nasopharynx	Speaker : Dr. Himanshu Pruthi (RADIOTHERAPY)
07/01/2021	• Unipath Speciality Laboratory Ltd's corporate brief, vision and way forward for genomics. • Developments in leukaemia: Significance on PH- like Chromosome	Speaker : Dr. Neeraj Arora (Post Doctoral Fellowship in Hematopathology & Molecular Hematology .) (CMC, Vellore) Speaker : Dr. Amisha Shah (Specialized training in cytogenetics and FISH at CMC, Vellore for 3 years.
14/01/2021	• CBK 4/6 inhibitor : Real World Experience.	Speaker : Dr. Rakesh Roy (MEDICAL ONCOLOGY)
21/01/2021	• Extravascation injury of Chemotherapeutic agents, management, & importance of Chemoport.	Speaker : Dr. Sudip Halder (SURGERY)
28/01/2021	• Radiotherapy with unsealed radioactive substance.	Speaker : Dr. M. Ariff (RADIO THERAPY)
04/02/2021	• Approach to Pancytopenia	Speaker: Dr. Tusti Ganguly (HEMATO ONCOLOGY)
11/02/2021	• Advanced Ostomy Care Management.	Speaker : Mr. Sudipta Das
18/02/2021	• Role of Protein and Omega 3 fatty acid in management of Cancer.	Speaker :Dr. Koyel Pal Chowdhury.
25/02/2021	• Neoadjuvant Therapy in Melanoma.	Speaker : Dr. Sudip Halder (SURGERY)

04/03/2021	• Rapid Arc Radiotherapy .	Speaker : Dr. M. Ariff (RADIO THERAPY)
11/03/2021	• Molecular targets in Lung Ca.	Speaker: Dr. Swarnabindu Banerjee (Consultant Haematologist, Calcutta Medical College & Hospital)
18/03/2021	• Basic of Solid Tumor & Hematological Malignancies.	Speaker: Dr. Arun Kumar (Scientific Affairs Manager, Med Genome Labs Ltd)
25/03/2021	• Role of IV fluids in pre & post Operative Onco Surgery.	Speaker : Dr. Sudip Halder (SURGERY)
01/04/2021	• Recent Advances in HER2 NEU Positive Breast Cancer Management.	Speaker : Dr. Sudip Halder (SURGERY)
22/04/2021	• Prostate Ca- Updates.	Speaker : Dr. Rakesh Roy (RADIO THERAPY)
29/04/2021	• Ca-Lung	Speaker : Dr. Himangshu Pruti (RADIO THERAPY)
06/05/2021	• Basic Immuno- Oncology & Clinical Importance.	Speaker : Dr. Sudip Halder (SURGERY)
13/05/2021	• Tackling the Pandemic among Cancer Patients One year Experience.	Speaker : Dr. Baijaeek Sain (SURGERY)
20/05/2021	• Carcinoma Endometrium Management .	Speaker : Dr. Hiamangshu Pruti (RADIO THERAPY) .
27/05/2021	• Ca- Cervix	Speaker : Dr. Hiamangshu Pruti (RADIO THERAPY) .
03/06/2021	• Neoadjuvant Therapy in Resectable Pancreatic Csncer.	Speaker:Dr.Radharaman Mondal (SURGERY)
10/06/2021	• Management of locally advanced Ca- Rectum.	Speaker: Dr. Saurav Banerjee (RADIO THERAPY) .
17/06/2021	• Morphin : Usage and local administration Laws.	Speaker : Dr. Kuntal Ghosh (PALLIATIVE CARE)
24/06/2021	• BMT Procedure in transplant and way forward.	Speaker: Dr. Rahul Bhargava. (Director: Fortis Hospital, Shalimar Bagh: Fortis Memorial & Research Institute, Gurgaon.)
01/07/2021	• Role of Radiation Therapy in Ca- Oesophagus.	Speaker : Dr. Sourav Banerjee (RADIO THERAPY) .
08/07/2021	• Medical Oncology guideline during Covid 19 Pandemic.	Speaker: Dr. Rakesh Roy (MEDICAL ONCOLOGY)
15/07/2021	• Testicular Ca	Speaker : Dr. Himanshu Pruthi (RADIO THERAPY)
22/07/2021	• Appendicular Ca.	Speaker : Dr. Baijaeek Sain (SURGERY)

29/07/2021	• An Experience in the Era of TKI Therapy.	Speaker : Dr. Somsubhra Nath (MOLECULAR BIOLOGY)
05/08/2021	• Fertility preservation before gonadotoxic therapy.	Speaker : Dr. Sudip Halder (SURGERY)
12/08/2021	• "Chasing the beast : Mutated TP53 in Gynaecological Ca.	Speaker :Dr. Damayanti Das Ghosh. (MOLECULAR BIOLOGY)
19/08/2021	• Ca - Oropharynx	Speaker : Dr. Himanshu Pruthi (RADIO THERAPY)
26/08/2021	• Osteosarcoma Maxilla	Speaker : Dr. Baijaeek Sain (SURGERY)
02/09/2021	• To smoke or not to smoke – that is the question: A search for genetic risk signatures for lung Cancer.	Speaker : Dr. Mainak Sengupta (Dept. Of Genetics, University of Calcutta)
09/09/2021	• The magic of High end Linac : 2D and 3D imaging.	Speaker : Dr. Sampuran Acharya (RADIO THERAPY)
16/09/2021	• PICCing up the right VAD in Oncology and Haematology.	Speaker : Dr. Tusti Ganguly Dr. Rakesh Roy (HEMATO ONCOLOGY, MEDICAL ONCOLOGY)
23/09/2021	• Ca Prostate	Speaker : Dr. Himanshu Pruthi (RADIO THERAPY)
30/09/2021	• Evolving Management of Brain Meastases.	Speaker : Dr. Jyotirup Goswami (RADIO THERAPY)
07/10/2021	• Overview of MDS	Speaker : Dr. Sudip Halder (SURGERY)
21/10/2021	• Radiotherapy in Pediatric Malignancy .	Speaker : Dr. Jyotirup Goswami (RADIO THERAPY)
28/10/2021	• A future, free of Breast Cancer	Speaker:Dr.Sumohan Chatterjee(UK) (Consultant Breast and reconstructive surgeon, Manchester University Foundation, NHS Trust)
04/11/2021	• Overview of MDS	Speaker : Dr. Tusti Ganguly (HEMATO ONCOLOGY)
11/11/2021	• Nutrition in Pediatric Cancer.	Speaker : Dr. Soma De (PEDIATRIC ONCOLOGY)
18/11/2021	• Overview of Iron deficiency in Anemia.	Speaker : Dr. Tusti Ganguly (HEMATO ONCOLOGY)

25/11/2021	• Panel Discussion on HER2 Positive Breast Ca.	Speaker : Dr. Rakesh Roy (MEDICAL ONCOLOGY)
02/12/2021	• Ca-Rectum & Role of Radiation, DNB@ SGCCRI – Untold Experience.	Speaker : Dr. Himanshu Pruthi (RADIO THERAPY)
09/12/2021	• Quality control in Laboratory .	Speaker : Dr. Shravasti Roy (PATHOLOGY)
16/12/2021	• "Current state of the art in Small Cell Lung Ca..	Speaker : Dr. Niladri Ghosal (UK)
23/12/2021	• Muscle Invasive Bladder Ca: Overview of Management.	Speaker:Dr.Radharaman Mondal. (SURGERY)
30/12/2021	• High Grade Glioma	Speaker : Dr. S.Tarun (RADIO THERAPY)

PANORAMA OF ACADEMIC ACTIVITIES

Dr Arnab Gupta

- Chairperson in a GI Oncology session at Mid Term Annual Conference of IASO at Tirupati in March, 2020.
- Chairperson in India Breast Cancer Symposium- Recent developments at Delhi in March, 2020.
- Chairperson in a session on `Biomarkers in Head & Neck Cancer` during the 3rd Annual Review on Head & Neck Cancers Conference (Virtual) in June, 2020.
- Chief Faculty for Masterclass on `Breast diseases: A Surgical Overview` organized by AIMSA & West Bengal Student Medical cell in June, 2020.
- Panelist in a session `De-escalation of `Anti- Her2neu therapy`during the 3rd Annual Gujarat Breast Conference in Aug, 2020.
- Panelist in a session on `Best Management of Breast Cancer at District level- pre & present Covid era` at ABSI conference organized by Jharkhand State ASI chapter in August, 2020.
- Guest lecture: `D2 Gastrectomy- State of the Art` in `Gastric Cancer Update 2020` organized by ASI, Chennai City Branch & IASO, in Sept, 2020.
- Master Video: `Skin & Nipple preserving Mastectomy`, JASICON (ASI Sate Conference of Jharkhand in Nov, 20
- Moderator of a Debate: `Need for Complete ALND for positive SLNB`, at JASICON in Nov, 20.
- Chairperson of a session on `Lap LAR` at Oncosurg, organized by IPGMER, Kolkata in Dec, 20.
- Master Video: `Liver Resection & Radical Cholecystectomy`, at ASICON, in Dec, 20.
- Chairperson for a Master Video session `D2 Gastrectomy- by Dr Takeshi Sano, Japan, at Eastern India Oncology Conclave (Theme: Controversies & Consensus in the Management of Upper GI cancers), a virtual conference hosted by Oncological Society of Bengal under the Aegis of IASO, in Dec, 2020
- Guest Lecture: `Guidelines by IASO during Covid 19` during the virtual NATCON (National Conference of IMA) in Dec, 2020.
- Chairperson for a session on `Recent advancements in Management of chronic wounds` at 1st Annual Conference `PTW-Con 2021` organized by `Protect the Warriors` held in Kolkata in March, 2021.
- Guest lecture on `Lifestyle, Environment & Cancer` at a Virtual International Health Conclave organized by Dr B C Roy Engineering College in April, 2021.
- Chairperson in Head & Neck cancer session of ISOCON Mid term conference held virtually in April, 2021
- Chairperson in a Webinar on `Low Rectal Cancer- Sphincter Preservation` organized by Oncology Society in Bangalore in collaboration with IASO in June, 2021.
- Judge for `Clinical Case Presentations` at Med- Invade 2021 organized by SMR in July, 2021.
- Chairperson for a talk on `Lung Cancer- recent developments` in an International Webinar on Respiratory diseases organized by Royal College of Surgeons, Edinburgh in August, 2021.

- Chairperson for 5 Orations in NATCON IASO in Delhi in Oct, 2021 as President of IASO.
- Judge of Award sessions in NATCON IASO in Oct, 2021 in Delhi.
- Keynote lecture on `Colorectal Liver metastases- current management`&`Management of Gastric cancer` in Odisha Society of Oncology (OSOCON) held in Bhubaneswar in Nov, 21.
- Panelist in a session on `Colorectal Liver metastases` in ASICON, 2021 (virtual) held in Dec, 21.

Dr Rakesh Roy

1. Selected as Principal Investigator: Study of PIK3CA Mutations and Effectiveness and Tolerability Outcomes of Alpelisib in Real -world (SPEAR), a multicentric trial involving 26 centres. The study has already been initiated.
2. Successfully completed "Executive Program on Leadership & Management" from IIM Calcutta and received the ALUMNI Status in 2020.
3. Successfully completed MBA – Hospital Management from the prestigious Annamalai University, Tamil Nadu in the year 2021.
4. Recertification – Good Clinical Practice in accordance with changing scenario during COVID 19 pandemic, July 2021.
5. For the third time in a row "Saroj Gupta Cancer Centre & Research Institute" has been declared as "ESMO Designated Centre of Integrated Oncology and Palliative Care" from the period 2022 – 2024 under the Leadership of Dr R Roy.

Dr Tamohan Chaudhuri

Department of Radiation Oncology

1. Centre Incharge plus Examiner in DNB (RT) final examination held at SGCC&RI, February 2021 External examiner in Formative Assessment examination for DNB (RT) held in Ruby Hospital, Kolkata in June 2021
2. Co-Investigator of Interlace trial (a multicentric global clinical trial)

Dr Abhijit Sarkar

Department of Radiation Oncology

1. Successfully completed MBA – Hospital Management from the prestigious Annamalai University, Tamil Nadu in the year 2021.
2. Successfully completed a course in Medical Law and Ethics (PGDMLE) , from National Law School of India University, Bangalore. 27th September 2020

Dr. Indranil Chatterjee

1. Successfully completed the Post Graduate Diploma in Medical Law and Ethics from prestigious National Law School Bangalore in 2020.
2. Successfully completed Post Graduate Diploma in Healthcare Management, with Distinction from Welingkar Institute, Mumbai in September –October 2021.

Academic Awards and recognitions from Basic & Translational Research Division

SGCCRI has been recognised as a "Sister Institute" of University of Calcutta for conducting PhD programme

- Prof. Susanta Roychoudhury, Chief, Basic Research, has been awarded the Emeritus Scientist Fellowship from Indian Council of Medical Research (ICMR), Govt. of India
- Prof. Susanta Roychoudhury, Chief, Basic Research, has been elected as a J.C. Bose National Fellow of Dept of Science and Technology, Govt. of India
- Prof. Susanta Roychoudhury has been elected as a Fellow of the India National Science Academy
- Dr. Somsubhra Nath elected associated member of West Bengal Academy of Science of Technology. Dr. Somsubhra Nath, Scientist, Basic Research, received Early Career Research Award from Science and Engineering Research Board, Govt. of India
- Dr. Somsubhra Nath received an Extra Mural Research Grant from Dept of Higher Education, Science, Technology and Biotechnology, Govt. of West Bengal
- Dr. Somsubhra Nath received Shri Ramnath Jaju Award for Best Oral Presentation for Mid-level Scientists at 39th Annual Conference of Indian Association of Cancer Research (IACR), 2020
- Dr. Damayanti Das Ghosh received the grant under the scheme of DST-Woman Scientist A
- Ms. Stuti Roy has been awarded Senior Research Fellowship from University Grants Commission-National Eligibility Test (UGC-NET)
- Mr. Suryendu Saha has been awarded Senior Research Fellowship from DST-INSPIRE scheme, Govt. of India
- Mr. Ratnadeep Paul has been awarded Junior Research Fellowship from ICMR, Govt. of India

Achievements

Dr Arnab Gupta

Elected President of Indian Association of Surgical Oncology (2019-2021)

Selected as Advisor of National Institute of Pharmaceutical Education and Research

Dr. Biman Chakraborty

Dr Saroj Gupta LifeTime Achievement Award.

In Recognition To His Dedicated Service To This Institute. (5th Dec 2020)

Dr Radheshyam Majumdar

Dr Saroj Gupta Lifetime Achievement Award.

In Recognition To His Dedicated Service To This Institute. (5th Dec 2021)

Dr Y Vishnu Reddy

Successfully Completed DNB Radiotherapy

Dr Roopesh Reddy

Successfully Completed DNB Radiotherapy

Dr Sanchayan Mandal

Successfully Completed DNB Radiotherapy

Dr Syed Hassanuzzaman

Successfully Completed DNB Surgical Oncology

Dr P Bharath, Dr. M. Santhosh

Successfully Completed DNB Surgical Oncology

Events of 2021 (January to December)

Inaugurations:

Multipara Monitor (15th Jan, 2021)

1 number Multipara Monitor & 2 number Pulse Oximeters were donated by Mr Sanjay & Mr Ashok Agarwal for the Emergency Ward of SGCCRI. These medical equipment were essential for monitoring the critical cancer patients attending our Emergency department, before being shifted to our ICU. Inauguration of Covid 19 Vaccine Centre (25th Jan, 2021) The Institute got actively involved in helping the Society in Vaccination against Covid- 19 from Day 1 of the Govt initative. Since then all the Staff of SGCCRI, many other Healthcare & Frontline workers from different parts of the city and later on the 18+ population got vaccinated here. The ambience and the Covid safety protocol were appreciated by all including the Govt of West Bengal.

World Cancer Awareness Day (4th February, 2021)

Thursday, 4th February 2021, **World Cancer Awareness Day** was celebrated in our Institute by Inaugurating 3 Portable & 1 Static X-Ray machines donated by Balmer Lawrie & Co Ltd, under their CSR initiative.

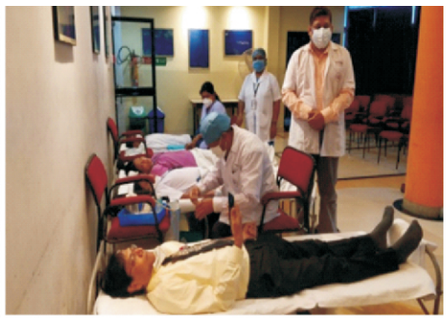
'Rotary Club Calcutta Universe' & 'Rotary Club of Rabindra Sarobar' distributed Toys to the child patients & donation to this Institute.

'Rotary Club of Ballygunge South' and 'Behala Mahila Mondal' distributed gifts to the Child patients admitted in this Institute.

11th International Childhood Cancer Awareness Day (15th Feb, 2021)

This year **CanKids KidsCan**, an NGO, celebrated International **'Childhood Cancer Awareness Day'** with SGCCRI. They celebrated the day with child patients & their mothers in SGCCRI Child Care Centre. The highlights of the programme were drawing competition, Prize distribution, Cake cutting & Gift distribution for children. The programme aimed at building awareness to promote deeper understanding of the challenges faced by children and adolescents suffering from cancers along with their care givers.

11th Anniversary of Dr. Saroj Gupta (21st May, 2021)

11th Anniversary of our Founder Late **Dr. Saroj Gupta** was observed on 20th May, 2021. A Blood Donation camp was held in-house. Many of our Management, Staff and patient-relatives voluntarily donated blood for our patients.

In House Blood Donation Camps in support of Patients at our Hospital in 2021

To meet the acute shortage of Blood for our In-patients, **SGCCRI Blood Bank organized in-house Blood Donation Camps in its own- premises**. Many of our staff came forward to donate "the gift of life" (Blood) for the Paediatric & adult patients admitted in this Institute.


4 no Jumbo Oxygen Cylinders along with 4 no Flow Meters donated by Rotary Club of Kolkata Galaxy on 7th August, 2021. Tree Plantation & Donation of 4 no Jumbo Oxygen Cylinders were done by 'Rotary Club of Cosssipore' on 4th Nov, 2021.

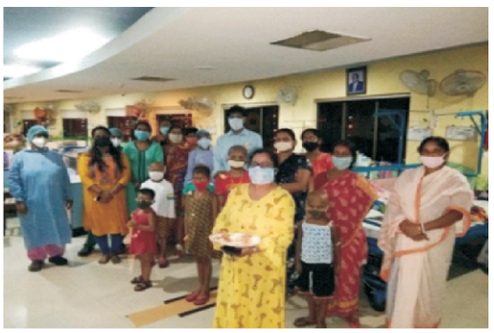
Independence Day (15th August, 2021)


Independence Day was celebrated like every year with Flag hoisting. Members of Management, Staff and patient-relatives were present there to pay tribute to our Freedom fighters.

Inauguration of Flow Cytometer in the Molecular Biology Department
(7th Sept, 2021)

'**Flow Cytometer**', which was donated by Switz Foods Pvt Ltd, was inaugurated in the Molecular Biology division of SGCC&RI by the owners **Mr. Taizoon Khorakiwala**, **Mrs Edith Khorakiwala** along with **Mrs. Pratima Basu**. **Mr. Mohan Krishna Maitra**, General Manager, **Switz Foods Pvt Ltd** was also present along with the members of the Management.

Project 'Gold Light up' at SGCCRI by CanKids (15th Sept, 2021)



'**Gold' has been selected as the color of Childhood Cancer**. The colour embodies strength, courage and resilience of all the children diagnosed with cancer and their families. In recognition of the children fighting cancers **CanKids KidsCan organized a programme** in the SGCCRI Child Care Centre on September 15, 2021 as part of Childhood Cancer Awareness Month.

The children along with their care givers participated with Gold Ribbons in recognition of their strength to fight Cancer. The Child Care Centre was illuminated with Golden coloured lights creating a very special ambience against the night sky.

Diwali Celebration (2nd Nov, 2021) CanKids, an NGO organized a colourful
'Diwali' for the children of SGCCRI.

Children's Day Celebration (15th Nov, 2021)

The Hospital has been celebrating Children's Day in a big way since 2002 to bring back smiles on the faces of children suffering from cancer. On 15th November, 2021 for the 20th consecutive year, we have celebrated Children's day with **Rotary Club Calcutta Metropolitan, Rotary Club Calcutta South Circle, Rotary Club Calcutta Lansdowne** and **Rotaractors of Dist 3291** on the 1st floor of the Child Care Centre. Members of **Rotary Clubs & many individuals** made personal donations to the Institute.

Press Conference at The Press Club Maidan Tent for 75 Successful BMTs, (16th Nov, 2021)

A Special Press Conference was organized by Saroj Gupta Cancer Centre & Research Institute for the **attainment of an extraordinary landmark by completing the 75th Bone Marrow Transplantation of our cancer patients at SGCCRI**. We earnestly solicited the involvement of the print & digital media for publicity of this achievement and broadcasting this unique facility being offered to all cancer victims.

Inauguration of PSA (Oxygen Plant) (19.11.2021)

A PSA (Oxygen Plant) was funded by '**Garden Reach Ship Builders & Engineers Ltd**' under their CSR initiative was inaugurated by **Commodore PR Hari, IN (Retd.), Director (Personnel), Mr S Srinivas,** with **GM (HR & A), Mrs Lipi Das, Addl. GM (ER &A), GRSE Ltd with Mr. Anjan Gupta**, Hony Secretary, **Dr Arnab Gupta,** Director and **Dr Gautam Bhattacharjee,** Asst Secretary & HOD Radiotherapy of **SGCCRI** at this hospital .

The Founder's Day (5th December, 2021)

Founder's day was observed on **5th December, 2021, the 92nd Birth Anniversary of our Founder Dr Saroj Gupta**. Blood Donation Camp was organized on 4th December, 2021 in the morning where members of the Management and many staff donated blood. **Dr Radheshyam Majumdar (eminent Cardiologist) & Shri Subhash Guha Niyogi, Past President Agri-Horticultural Society,** senior most governing body members, both aged 93 were felicitated with **'Dr Saroj Gupta Life Time Achievement Award'** for this year in recognition of their dedicated service to this Institute and both have been actively involved in the development of the Hospital since its inception.

HDR Brachytherapy & Plasma Sterilizer, donated by Indian Oil Petronas Private Limited (under their CSR initiative), were inaugurated by **Shri Pradip Kumar Jha,** CEO, IPPL along with **Mr Mazlie Bin Minhat,** FC, IPPL in presence of the Management of SGCCRI.

This was followed by the Release of **'The Journey'**, a Biopic of **Dr Saroj Gupta** directed by **Mr Arijit Mukherjee** of Arijit Official.

Publication

Manuscript type: Observational study

Title: An observational study to evaluate the response and toxicity with Conventional fractionation and hypofractionated radiotherapy for locally advanced NSCLC following induction chemotherapy.

Department(s) and institution(s): Department of Radiotherapy, Saroj Gupta Cancer Centre and Research Institute, Kolkata, West Bengal, India

Details of author(s):

1. Dr. Sujata Sarkar, MBBS, DNB Radiotherapy, Department of Radiotherapy, SGCCRI
   Email- sujatasarkar1989@gmail.com
2. Dr. Gautam Bhattacharjee, MD Radiotherapy, Department of Radiotherapy, SGCCRI
   Email- gautam.emgeebee@gmail.com
3. Dr. Tamohan Chaudhuri, DMRT, MD Radiotherapy, Department of Radiotherapy, SGCCRI
   Email- tamohanchaudhuri@yahoo.com

An Observational Study To Evaluate The Response And Toxicity With Conventional Fractionation and Hypofractionated Radiotherapy For Locally Advanced NSCLC Following Induction Chemotherapy

ABSTRACT:

Aims & Objectives: To evaluate the response and toxicity with Conventional fractionation and hypofractionated radiotherapy for locally advanced NSCLC following induction chemotherapy. To assess and compare following for locally advanced NSCLC with Conventional and hypofractionated radiotherapy following induction chemotherapy. **Materials And Methods:** This prospective observational study was conducted at Saroj Gupta Cancer Centre and Research Institute, Kolkata; accrual was from June 2016 to September 2017. Data was collected from all patients who had been cytological / histopathologically and radiological proven stage III Non Small Cell Lung Carcinoma; fulfilling eligibility criteria, were recruited after obtaining informed consent.

Results And Analysis: We found that the association between response at the END OF RT in two groups was not statistically significant (p=0.8559).? Association between Dermatitis highest grade at end of RT in

two groups was not statistically significant (p=0.5201). Association between Response 6 months after RT in two groups was not statistically significant (p=0.7667). Association between Dermatitis 9 months after RT in two groups was not statistically significant (p=0.9255).

Conclusion & Summary: Our study showed hypofractionated radiotherapy is non-inferior to Conventional radiotherapy with equivalent overall response and toxicity and well tolerable.
In patients with poor performance status who cannot tolerate concurrent chemo radiation, induction chemotherapy with hypofractionated radiotherapy regimen can be considered as a treatment of choice with manageable toxicities.

Keywords: Conventional fractionation, Hypofractionated radiotherapy, Non small cell lung carcinoma, Induction chemotherapy.

INTRODUCTION:

Lung cancer is one of the most common cancers and also the most common cause of cancer related deaths worldwide1. In 2008 there were 1.61 million new cases, and 1.38 million deaths due to lung cancer, and it has increased to 1.8 million new cases in 2012 (12.9% of the total) which estimated to be responsible for nearly one in five (1.59 million deaths, 19.4% of the total) 2. The highest rates are in Europe and North America. With increased smoking in developing countries, the rates are expected to increase in the next few years, notably in India3 and China. In India, lung cancer constitutes the second most common cancer in male and contributes to significant mortality in both male and female. The incidence of lung cancer in India is 70,000 per year, out of which mortality is 64000 per year. Majority of the patients are detected with non-small cell lung cancer (NSCLC) with a mean age of diagnosis at 66 years, i.e., it is a disease affecting the elderly people. In developed countries, lung cancer patients usually present in early stage; while in developing countries like India, they present in locally advanced stage (stage III) 2. Lung cancer is broadly classified into small cell lung carcinoma and non-small cell lung carcinoma. Non-small cell lung cancer constitutes 75-80% of all lung cancers. More than 70% of them are in Stage III and IV when diagnosed making curative surgery difficult. Small cell lung carcinoma which constitutes 20% is in the extensive stage when diagnosed in 70% of patients. This distinction is important because the treatment varies; small cell lung carcinoma (SCLC)

usually responds better to chemotherapy, non-small cell lung carcinoma (NSCLC) is treated with surgery in the early stages, but in locally advanced (stage III) cases combined modality treatments are practiced in recent days, like concurrent chemo radiation therapy, systemic chemotherapy and radiotherapy to residual disease, radiation therapy alone, sequential chemo radiation therapy. In concurrent chemo radiation therapy, it can be induction/ concurrent, and/ or concurrent/ consolidation.

At Saroj Gupta Cancer Centre & Research Institute (SGCC&RI), locally advanced non metastatic non-small cell lung cancer patients are mostly elderly with co-morbidities (e.g. diabetes mellitus, hypertension etc.) having commonly poor(>1) Eastern Co-operative Oncology Group (ECOG) Performance Status (PS). Those patients are deemed inappropriate for concurrent chemoradiation due to the anticipated toxicities and poor tolerance. They are treated with sequential chemoradiation using either Conventional or hypofractionated radiation therapy based upon the decision of tumor board. Radiation therapy is given mainly as a daycare based procedure and hypofractionated radiation therapy is preferred for patients coming from distant places in view of early completion of treatment. Although enough trials are there to justify the use of hypo-fractionated radiotherapy in locally advanced NSCLC, till now there is no Indian data regarding the same4.

We have a huge number of patients coming with locally advanced NSCLC at our institution and it seems prudent to conduct a study observing the response and toxicity of the two radiotherapy schedules; to evaluate the response and toxicity with Conventional fractionation and hypofractionated radiotherapy for locally advanced NSCLC following induction chemotherapy. To assess and compare following for locally advanced NSCLC with Conventional and hypo fractionated radiotherapy following induction chemotherapy-Response assessment at the end of treatment and at 3 months, 6 months and 9 months using Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 criteria17.

1. Toxicity assessment (radiation dermatitis, esophagitis, pneumonitis) at the end of treatment and at 3 months, 6 months and 9 months after completion of radiation using Radiation.
2. Additionally, Disease Free Survival and Progression Free Survival at 3 months, 6 months, 9 months after completion of treatment.

MATERIALS AND METHODS:

Source of Data:-

This prospective observational study was conducted at Saroj Gupta Cancer Centre and Research Institute, Kolkata; accrual was from June 2016 to September 2017. Data was collected from all patients who had been cytological / histopathologically and radiological proven stage III Non Small Cell Lung Carcinoma; fulfilling eligibility criteria, were? recruited after obtaining informed consent.

Inclusion Criteria:

i) Biopsy/cytology proven Stage III NSCLC
ii) No prior history of malignancy
iii) ECOG PS >1 who are unfit for concurrent chemoradiation
iv) No prior radiotherapy, chemotherapy or surgery for disease
v) Age <80 years of either sex
vi) Weight loss >5% over 3months
vii) No distant metastasis
viii) LVEF >60%
ix) BUN <25mg/dl
x) Serum creatinine <1.5mg/dl
xi) Serum bilirubin <1.5mg/dl
xii) Baseline Hemoglobin > 10 gm/dl
xiii) Absolute Neutrophil Count > 1500/µl
xiv) Platelets > 1, 00,000/µl.
xv) Has signed written informed consent.

Exclusion Criteria:

i) Patients with age > 80 years
ii) Patients with clinical or radiological evidence of distant metastasis.
iii) Patients who are restless being unsuitable for radiation therapy
iv) Patients with pregnancy or breast feeding
v) Patients with history of allergic reaction to iodinated contrast media
vi) Patients who have participated in any other study on lung cancer.
vii) Patient's refusal to undergo chemotherapy and/or radiotherapy.

Treatment Plan

Radiotherapy Protocol STUDY TOOLS:

Case Performa, standard hematological, biochemical and radiological investigations

i. Siemens Somatomscope 16 slice helical CT scanner
ii. Siemens Primus Linear Accelerator (LINAC) single energy 6MV with 29 pairs of multileaf collimators
iii. Oncentra v4.3– treatment planning system (developed by Nucletron and maintained by Elekta)
iv. Inj. Paclitaxel (175mg/m2) with necessary premedication and fluids
v. Inj. Carboplatin (AUC5) with necessary premedication and fluids

RESULTS AND ANALYSIS:

Our study showed that the difference of mean age in two groups was not statistically significant. Thus age was matched in two groups. There was no statistically significant difference in age distribution between the groups. Numerical variables between groups compared by t-test; (p=0.7452). Association between age in two groups was not statistically significant (p=0.4430). Association between sex in two was not statistically significant (p=0.7232). Association between ECOG PS in two groups was not statistically significant (p=0.9298). Distribution of stage in two groups was not statistically significant (p=1.000). Association between histopathology in two groups was not statistically significant (p=0.3111). Association between comorbidity in two groups was not statistically significant(p=0.4308). Association between habit in two groups was not statistically significant (p=0.1417). Association between tumor size in two groups was not statistically significant (p=0.3705). Association between lymph node involvement in two groups was not statistically significant (p=0.9402). All the patients had received induction chemotherapy in both groups.

We found that the association between response at END OF RT in two groups was not statistically significant (p=0.8559). Association between Response 3 months after RT in two groups was not statistically significant (p=0.7659). Association between Response 6 months after RT in two groups was not statistically significant (p=0.7667). Association between Response 9 months after RT in two groups was not statistically significant (p=0.9255). Association between Dermatitis highest grade at end of RT in two groups was not statistically significant (p=0.5201). Association between Esophagitis highest grade at end of RT in two groups was not

statistically significant (p=0.4283). Association between Pneumonitis highest grade at end of RT in two groups was not statistically significant (p=1.000). Association between Dermatitis 3 months after RT in two groups was not statistically significant (p=0.5968). Association between Dermatitis 6 months after RT in two groups was not statistically significant (p=0.31118). No patient had dermatitis 9 months after RT. Association between Esophagitis 3 months after RT was not statistically significant (p=0.3421). Association between Esophagitis 6 months after RT was not statistically significant (p=0.3111).

DISCUSSION

The present study was undertaken in Department of Radiotherapy, SGCC & RI, Kolkata. The patients with newly diagnosed, histological proven stage IIIA and IIIB lung cancers were presented in hospital tumor board and after board decision, treatment was decided.

Epidemiological Comparison:

In this study, approximately 95% of patients were more than 50 years of age at presentation with median age of 72 years in “Conventional arm” and 69 years in “hypo arm”. This is consistent with the expected age distribution ranging from 5th to 7th decades of life as quoted in literature by Yamamoto et al5 and Belani et al6; and with an average age of 68 years as quoted in literature. The incidence of lung cancer increases with age, especially after 60 years of age. Lung cancer is more common in males. In Analysis of data from 22 cancer registries in 5 continents revealed that cumulative lung cancer risks were higher in males than females. In our study, “Conventional arm” has 75% male and “hypo arm” has 70% male patients.

Cigarette smoking associated with an increased risk of lung cancers. Approximately 80% of cases of non-small cell lung cancer (NSCLC) in men and 50% of these neoplasms in women worldwide are directly attributable to cigarette smoking.

In a study by Amini et al7 92% of patients of his study group were smokers. Our study had only 50% smokers averaged over both groups. In a study by P. Iyengar et al8, 53% had Squamous Cell Carcinoma and 47% Adeno Carcinoma. In our study, approximately 70% squamous Cell and 30% Adeno Carcinoma averaged over both groups.

In most of the studies including those conducted byAmini et al7, there were no significant differences in the distribution of stages IIIA and IIIB between the two groups. In our study, 45% are Stage IIIA and 55% are Stage IIIB.

Induction chemotherapy was used in studies by P. Iyengar et al8, Din Os et al9 and Amini et al7 with hypofractionated Radiotherapy. In our study, Paclitaxel 175mg/m2 and Carboplatin AUC5 are used for induction chemotherapy.

Response Evaluation:

It has been shown time and again that sequential chemo-radiotherapy is a good treatment option for patients with Stage III NSCLC who are unsuitable for concurrent chemoradiation due to older age, poor performance status and medical co-morbidities. Lung Cancer is a disease of older age group and most of the patients cannot tolerate the toxicities of concurrent chemo-radiation as shown by the landmark trial of RTOG 9410 where less than 30% of Stage III NSCLC patients were unfit for concurrent chemo-radiation4, which is also supported by D. De Ruysscher10 et al and in Indian context. Such patients are often non-compliant to prolonged 6 weeks standard radiation protocol. Hypofractionated Radiotherapy is an effective protocol owing to early termination of radiation keeping them moreadherent to treatment. Radiobiologically also hypofractionation prevents accelerated tumor repopulation by virtue of early completion of treatment.

In our study, we reported the overall treatment response rates between the Conventional RT group and the hypo fractionated RT group at the end of treatment, at 3 months, 6 months and 9 months after completion of treatment.

A study by Nguyen LN et al 8 showed that hypofractionated group had 14% CR, 38% PR while Conventional group had 25% CR, 42% PR.

In a study by Zhu ZF et al11 the median and 3-year overall survival, PFS were 19 months in 32.1% and 10 months in 29.8%, respectively. The 1, 2 and 3-year LR-PFS were 69.6%, 60.9% and 60.9% respectively. No patient experienced isolated elective nodal failure as the first site of failure. This study suggested that accelerated Hypofractionated radiotherapy using 3D-CRT omitting ENI can be used in combination with sequential chemotherapy in locally advanced NSCLC.

CONCLUSION AND SUMMARY:

Our study showed hypofractionated radiotherapy is non-inferior to Conventional radiotherapy with equivalent overall response and toxicity and well tolerable.

In patients with poor performance status who cannot tolerate concurrent

chemo radiation, induction chemotherapy with hypofractionated radiotherapy regimen can be considered as a treatment of choice with manageable toxicities.

There was no statistical difference between Conventional and hypofractionated radiotherapy for locally advanced NSCLC as far as tumor control and toxicities were concerned.

All toxicities occurred in our study were well manageable with best supportive care.

A prospective randomized study with large number of patients and longer period of follow-up is needed to extract safe conclusion about the superiority of Conventional vs hypofractionated radiotherapy.

The study titled “Observational Study To Evaluate The Response And Toxicity With Conventional Fractionation And Hypofractionated Radiotherapy For LocallyAdvanced Non-Small Cell Lung Carcinoma Following Induction Chemotherapy”, was performed in the department of Radiotherapy, Saroj Gupta Cancer Centre & Research Institute, Kolkata from June 2016 to September 2017.

40 patients of non-small cell lung cancers of stage IIIA & IIIB satisfying the eligibility criteria were enrolled for the study. In this study, we had given induction chemotherapy [3 weekly Paclitaxel (175 mg/m2) / Carboplatin (AUC5) for 3 cycles] followed by radiotherapy either in Conventional fractionation or Hypofractionated radiotherapy. The radiation dose delivered in Conventional fractionation was 60Gy in 30 fractions (2 Gy/fraction, 5 days/week) in

6 weeks. The radiation dose delivered in Hypofractionated radiotherapy was 55Gy in 20 fractions (2.75Gy /fraction, 5 days/week) in 4 weeks.

Table 1: Distribution of Stage in Two Groups

GROUP RT **STAGE**	**Conventional**	**Hypofractionated**	**TOTAL**
IIIA	9	9	18
Row %	50.0	50.0	100.0
Col %	11	11	45
Row %	50.0	50.0	
Col %			
TOTAL	20	20	40
Row %	50.0	50.0	100.0
Col %20			

Table 2: Distribution of Histopathology in Two Groups

	GROUP RT		
HISTOPATHOLOGY	**Conventional**	**Hypofractionated**	**TOTAL**
Adenocarcinoma	8	5	13
Row %	61.5	38.5	100.0
Col %	40.0	25.0	32.5
Squamous cell carcinoma	12	15	27
Row %	44.4	55.6	100.0
Col %	60.0	75.0	67.5
TOTAL	20	20	40
Row %	44.4	55.6	100.0
Col %	100.0	100.0	100.0

REFERENCES:

1. Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D et al. Global cancer statistics. CA Cancer J Clin. 2011 Mar-Apr;61(2):69-90. doi: 10.3322/caac.20107.
2. GLOBOCAN 2012: Estimated Cancer Incidence, Mortality and Prevalence Worldwide in 2012. Retrieved fromhttp://globocan.iarc.fr/Pages/fact_sheets_ Cancer.aspx
3. Behera, D; Balamugesh T "Lung cancer in India" Indian Journal of Chest Diseases and Allied Sciences (2004); 46 (4): 269–81.
4. Curran WJ Jr, Paulus R, Langer CJ, Komaki R, Lee JS, Hauser S et al. Sequential vs concurrent chemoradiation for stage III non-small cell lung cancer: randomized phase III trial RTOG 9410. J Natl Cancer Inst. 2011 Oct 5;103(19):1452-60.doi:10.1093/jnci/djr325. Erratum in: J Natl Cancer Inst. 2012 Jan 4;104(1):79. PubMed PMID: 21903745.
5. Nobuyuki Yamamoto, Kazuhiko Nakagawa, Yasumasa Nishimura, Kayoko Tsujino, Miyako Satouchi, Shinzoh Kudo et al. Phase III Study Comparing Second- and Third Generation Regimens with Concurrent Thoracic Radiotherapy in Patients with Unresectable Stage III Non Small-Cell Lung Cancer: West Japan Thoracic Oncology Group WJTOG0105. J Clin Oncol2010; 28(23):3739-45.
6. Belani CP, Choy H, Bonomi P, Scott C, Travis P, Haluschak J, et al.

Combined chemoradiotherapy regimens of paclitaxel and carboplatin for locally advanced non small-cell lung cancer: a randomized phase II locally advanced multi-modality protocol. J Clin Oncol. 2005;23:5883–91.

7. Amini A, Lin SH, Wei C, Allen P, Cox JD, Komaki R et al. Accelerated hypofractionated radiation therapy compared to Conventionally fractionated radiation therapy for the treatment of inoperable non-small cell lung cancer. Radiat Oncol. 2012; 7:33.
8. P. Iyengar, K D. Westover, L. E. Court, M. K. Patel, A. T. Shivnani, M. W. Saunders et al - A Phase III Randomized Study of Image Guided Conventional (60Gy/30fx) vs Accelerated, Hypofractionated (60Gy/15fx) Radiation for Poor Performance Status Stage II and III NSCLC Patients –An Interim Analysis. International Journal
9. Din OS, Harden SV, Hudson E, Mohammed N, Pemberton LS, Lester JF et al Accelerated hypo-fractionated radiotherapy for non small cell lung cancer: results from 4 UK centres Radiother Oncol. 2013Oct;109(1):8-12.doi:10.1016/j. radonc.2013.07.014. Epub 2013 Oct 3.
10. De Ruysscher D, Botterweek A, Dirx M , et al: Eligibility for concurrent chemotherapy and radiotherapy of locally advanced lung cancer patients: a prospective population based study. Ann Oncol 2009; 20: pp. 98-102.
11. Zhu, Z. F., Ma, H. L., Fan, M. et al(2014). Sequential chemoradiotherapy with accelerated hypofractionated radiotherapy compared to concurrent chemoradiotherapy with standard radiotherapy for locally advanced non-small cell lung cancer. Technology in Cancer Research and Treatment, 13(3), 269- 275. DOI: 10.7785/tcrt.2012.500375.

ORIGINAL WORK PUBLISHED IN JOURNALS.

- Mathur P, Sathiskumar K, Chaturvedi M, Das P, Sudarshan K L, Santhappan S, Nallasamy V, John A, Narasimhan S, Roselind F S, . Cancer Statistics, 2020: Report From National Cancer registry Programme, India.ascopubs.org by 106.51.241.169 on July 16, 2020 from 106.51.241.169
- Bhattacharyya S, Gupta A. Colorectal Liver Metastasis: Current Concepts. Indian J Surg (2020). https://doi.org/10.1007/s12262-019-02051-7
- Mandal PK, Adhikari A, Biswas S, Giri A, Gupta A, Bhattacharya A. Comparasion of histopathological grading and staging of breast cancer with p53-positive and transforming growth factor-beta receptor 2-negative immunohistochemical marker expression cases. Cancer Transl Med 2020;6:30-3.
- Roychowdhury A, Samadder S, Das P, Mazumder DI, Chatterjee A, Addya S, Mondal R, Roy A, Roychoudhury S, Panda CK. Deregulation of H19 is associated with cervical carcinoma. Genomics. 112: 961-970 (2020)
- Islam MS, Dasgupta H, Basu M, Roy A, Alam N, Roychoudhury S and Panda CK. Reduction of nuclear Y654-p-β-catenin expression through SH3GL2-meditated downregulation of EGFR in chemotolerance TNBC: Clinical and prognostic importance. J Cell Physiol. 2020;1–15. https://doi.org/10.1002/jcp.29466
- Basu M, Ghosh S, Roychowdhury A, Samadder S, Das P, Addya S, Roy A, Pal DK, Roychoudhury S, Ghosh A, Panda CK. Integrative genomics and pathway analysis identified prevalent FA-BRCA pathway alterations in arsenic-associated urinary bladder carcinoma: Chronic arsenic accumulation in cancer tissues hampers the FA-BRCA pathway. Genomics. 2020 Nov;112(6):5055-5065. doi: 10.1016/j.ygeno.2020.09.012
- Ghatak D, Ghosh D D, Roychoudhury S. (2021) Cancer Stemness:p53 at the Wheel.Front.Oncol.10:604124.doi:10.3389/fonc.2020.604124
- Jena S, Bhattacharyya S, Gupta A, et al. (July 18, 2021) Axillary Reverse Mapping in Patients Undergoing Axillary Lymph Node Dissection: A Single Institution Experience From India. Cureus 13(7): e16462. doi:10.7759/cureus.16462
- Ghosh D D. TP53 mutations differentially affect prognosis of endometrial cancer: an in-silico approach. IGCS 2021
- Datta A, Guha P, Rathi M, Chaudhuri T. Theory of mind deficit in women with breast cancer and depression: A comparative study. Indian J Cancer 0;0:0.
- Mandal P, Bhattacharjee B, Sen S, Bhattacharya A, Saha S S, Roy Chowdhury R, Mondal N R, Chakrabarty B, Chatterjee T, Roy S, Sengupta S. Predominance of genomically defined a lineage of HPV16 over D lineage in Indian patients from eastern India with squamous cell carcinoma of the cervix in association with distinct oncogenic phenotypes. https://doi.org/10.1016/j.tranon.2021.101256.
- Kurtz JE, Gebski V, Sukhin V,….Roy Chowdhury R, ….et.al. Incorporating patient centered benefits as endpoints in randomized trials of maintenance therapies i…, Gynecological Oncology, https://doi.org/10.1016/j.ygyno.2021.02.018
- Ghatak D, Datta A, Roychowdhury T, Chattopadhyay S, Roychoudhury S. MicroRNA-324-5p-CUEDC2 Axis Mediates Gain-of-Function Mutant p53-Driven Cancer Stemness. Mol Cancer Res. 2021 Oct;19(10):1635-1650. doi: 10.1158/1541-7786.MCR-20-0717
- Rao M, Venkatraman P, Mukhopadhyay D, Roychoudhury S, Vanderford NL, Rangnekar VM. Value added by an inter-continental cancer consortium. Genes Cancer. 2021 May 21;12:65-68. doi: 10.18632/genesandcancer.215. eCollection 2021
- S Ghuwalewala, D Ghatak, S Das, S Roy, P Das, M Butti, R Gorain, S Nath, GC Kundu, S Roychoudhury. MiRNA-146a/AKT/β-catenin activation regulates cancer stem cell phenotype in oral squamous cell carcinoma by targeting CD24. Fronts Oncol (2021), doi: 10.3389/fonc.2021.651692
- Sengupta D, Banerjee S, Mukhopadhyay P, Mitra R, Chaudhuri T, Sarkar A, Bhattacharjee G, Nath S, Roychoudhury S, Bhattacharjee S, Sengupta M. A comprehensive meta-analysis and a case-control study give insights into genetic susceptibility of lung cancer and subgroups. Sci Rep. 2021 Jul 16;11(1):14572. doi:

10.1038/s41598-021-92275-z. PMID: 34272429.

- Dey S , Bhattacharyya D, Gupta P P, Nath S, Long-term Outcome of Philadelphia Chromosome Positive Leukemia from East-ern Indian Sub-continent: An Experience in the Era of Tyrosine Kinase Inhibitor (TKI) Therapy, Clinical Lymphoma, Myeloma and Leukemia (2021), doi: https://doi.org/10.1016/j.clml.2021.06.026

Original work in form of presentation paper in various conference

- Nath S. Investigating the molecular connection between harmone receptor status and ploidy management in breast cancer.https://doi.org/10.1016/j.annonc.2020.03.199

Published Review articles

- Somashekhar S.P, Acharya R, Saklani A, Parikh D, Goud J, Dixit J, Gopinath K, Kumar M.V, Bhojwani R, Nayak S, Rao S, Kothari K, Chandramohan K, Desai S, Gupta A. Adaptation and Safety Modifications to Perform Safe Minimal Access Surgery (MIS: Lapraroscopy and Robotics) During the Covid-19 Pandemic: Practice Modifications Expert Panel Consensus Guidelines from Academic of Minimal Access Zsurgical Oncology (AMASO)
- Ghatak D, Das Ghosh D, Roychoudhury S. Cancer Stemness: p53 at the Wheel. Front Oncol. 2021 Jan 11;10:604124. doi: 10.3389/fonc.2020.604124. eCollection 2020.
- Saha S, Dey S Nath S (2021). Steroid Hormone Receptors: Links With Cell Cycle MachineryandBreastCancerProgressionFront.Oncol.11:620214.doi:10.3389/fonc.2021.620214
- Ferreira A, Are Chandrakanth O, Gupta A. Co- Author of Editorial – Global Health Services Research. Global Forum of Cancer Surgeons: Support for the Brazilian Society of Surgical Oncology Journey towards Implementation of Cytoreductive Surgery/Hyperthermic Intraperitoneal Chemotherapy in Brazil, in Annals of Surgical Oncology 18th Jan, 2021: Ann Surg Oncol https://doi.org/10.1245/s 10434-020-09527-x

Ph.D / MD / DNB / MSc Thesis / Dissertation
Ratnadip Paul (2021) , Samya Dey (2021) and Anupa Chattopadhyay (2021) are Ph.D students
Case presentations published in Journals

- Paul SS, Sahu SK, Chatterjee I. Non-recurrent laryngeal nerve- a surgical challenge.J.EVID.BasedMed.Healthc.2020:7(30),0000-0000.DOI: 10.18410/jebmh/2020/000
- Desai Sharad & Gupta Arnab . IASO COVID-19 Guidelines (Updated on 9th April 2020) . PMID: 32382218. DOI: 10.1007/s13193-020-01081-y
- Sain B, Gupta A, Bhattacharya S, Mondal R R, Haldar S, Roy Shravasti. Primary adenocarcinoma of the appendix presenting with fresh bleeding per rectum : A case report. (Accepted 3 August 2021)
- Bhattacharyya S, Gupta A, Ghosh S. Locally Advanced Gastric Cancer. [J Indian Med Assoc 2021:119(7):71-3]
- Sarkar S, Chaudhuri T, Roy S, Bose S. A rare synchronouns presentation of double primary malignancies-lung and prostate. J Can Res Ther 2021;17:1576-9.
- Sain B, Gupta A, Ghosh S, Mondal R R, Bhattacharyya S, Ghose A. Osteosarcoma of the maxilla presenting as a chronic pyogenic abscess. A case report (International Journal of Case Reports). www.elsevier.com/locate/ijscr https://doi.org/10.1016/j.ijscr.2021.106425. Accepted 16 September 2021

Book Chapter

- Chakraborty B, Mondal N.R, Roy Chowdhury R, Chatterjee T. Fertility Following Gynecological Cancer: Book Chapter in Practical Guide in Assisted Reproductive Technology: GG Mukherjee, G.Khastgir, S.Chatterjee eds: 2018 Jaypee Brothers Medical Publishers (P) Ltd:293-301.

- Nath S, Roy S. Genomic Instability in Carcinogenesis. The Role of Oxidative Stress. Springer Nature Singapore

NABH Accreditation

The Institute has been granted Certification under Pre- Accreditation Entry-Level- Hospital program by National Accreditation Board for Hospitals for its services w.e.f October 2018.

Within a record period of 9 months, through intensive training, improved teamwork and regular workshops, with required infra-structural changes, the Accreditation process was completed.

The teamwork from employees of all categories helped in the process of this transition of quality awareness and service delivery.

With this Accreditation the Institute can now build upon its brand for further Quality Certifications in the National and International arena.