ASSOCIATION OF RADIATION ONCOLOGISTS OF INDIA

Quarterly Newsletter

September 2025 I Vol 21 I Issue 03

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Radiation Oncologist 'G'

Homi Bhabha Cancer Hospital & Research Center- Muzaffarpur

AROICON Tamilnadu & Puducherry State Chapter Conference

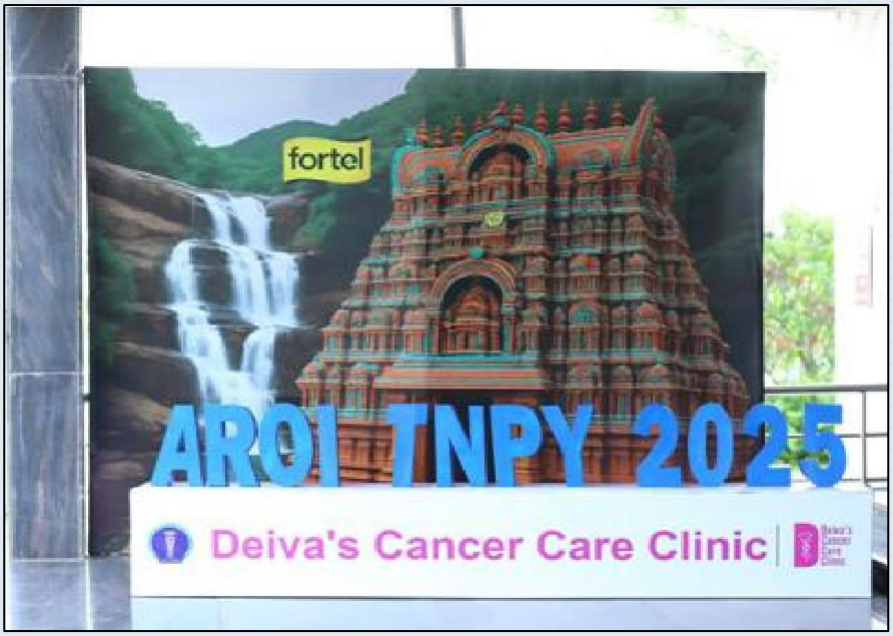
40th AROI TNPY 2025 Conference, the annual event for the Association of Radiation Oncologists of India (AROI), Tamil Nadu and Puducherry chapter was held at Green Royale Resorts, Courtallamon August 9-10, 2025 organised by Deiva's Cancer Care Centre and Department of Radiation Oncology,Tirunelveli Medical College. The conference was attended by 250 participants and close to 40 industry delegates from various institutions across Tamil Nadu and Puducherryand 81 abstracts were presented, including 28 oral presentations and 53 posters..

The Scientific session included Invited talks, Panel Discussion and Debates on all the major topics. Dr.Boopalan was the Chief guest for the Inaugural function and it was addressed by Dr. Balasundaram President AROI TN & PY, Dr.S.Balaji Secretary AROI TN & PY and Dr.Deivanayagam, Organising Chairman and Dr.Rajkumar Organising Secretary. Senior Radiation Oncologists Dr.Boopalan, Dr.M.Balu David, Dr.P.Balasubramaniam and Dr.S.Vijayaraghavan were felicitated by the Oraganising Chairman.

The Ida B. Scudder Oration delivered by Dr. SIMON PRADEEP PAVAMANI and the Prof. K. M. Rai Oration delivered by Dr. Sumana Premkumar.

The valedictory function recognized outstanding contributions by awarding all postgraduates who excelled in their oral and poster presentations. In a progressive initiative, AROI TNPY chapter instituted fellowships for students to observe high-technology radiotherapy practices at various centers; out of 10 applicants, 6 were selected to visit different centers across India.

Dr.S.Balaji	**Dr.V.Balasundaram**	**Dr.R.Deepak**
Secretary AROI TN & PY	**President AROI TN & PY**	**Treasurer AROI TN & PY**



Glimpses of AROICON TNPY 2025

AROICON Andhra Pradesh State Chapter Conference

AROICON for AP State chapter was consummated in a grand way spanning over a period of 2 days from 13/9/25 to 14/9/25; organised by Department of Radiation Oncology, at AIIMS MANGALAGIRI. The event was planned and executed in a seamless manner by the team of resident doctors and staff of the department under the leadership of DR KESAVA RAMGOPAL ORGANISING CHAIRMAN and DR SOOREJ BALAN K ORGANISING SECRETARY. The academic extravaganza was graced by experts and enthusiastic learners from all over the state in large numbers . Experts not only from state but eminent institutes of the country were invited by the organisers to share their insights and precepts with regards to HEAD AND NECK and PROSTATE malignancies. Panel discussions to workshop , with emphasis on contouring and RT planning, ensured active participation from the audience and the panel alike, which added to the distinctiveness of the academic fiesta. The 2 day program also included GBM of the AP AROI CHAPTER which was followed by a gala dinner at the Vijayawada club for an evening of socialising and networking. The organisers set a seal on interactive learning and wholesome entertainment for the delegates with a pinch of warm hospitality which culminated in , needless to say , massive success of the event

Dr Soorej Balan & Dr Kesava Ramgopal

50th ICRO PG Teaching Programme

Shri Guru Ram Rai University Hosts Golden Jubilee AROI ICRO PG Teaching Course

Shri Guru Ram Rai Institute of Medical and Health Sciences successfully hosted the prestigious 50th Golden Jubilee AROI ICRO Postgraduate Teaching Course from August 30-31, 2025. The theme of the course was Landmark clinical trials. The intensive two-day academic program brought together over 80 postgraduate students in Radiation Oncology from across the country to learn from leading national experts about the latest advancements in cancer treatment.

The event was inaugurated in a formal ceremony graced by a panel of distinguished dignitaries. Prof Dr Ashok Nayak, The Principal of the Medical College attended as the Chief Guest. He was joined on the dais by Dr. Senapati, President of the Association of Radiation Oncologists of India (AROI); President Elect Prof Dr. CS Madhu,; Dr. V. Srinivasan, Secretary of AROI; Dr. Sarbani, Chairman of the Indian College of Radiation Oncology (ICRO), Dr. Pooja Nandwani, Secretary of ICRO; and Dr. Manoj Gupta, the Organizing Chairman and Chair AROI, along with senior faculty members and FARO Advisor Dr. Rajesh Vashistha. The course was graced by presence of stalwart academicians Prof Dr GV Giri , and Dr S Pradhan, the past ICRO presidents.

In his welcome address, Organizing Chairman Dr. Manoj Gupta highlighted the course's legacy and its importance in shaping the future of oncology. "This Golden Jubilee course is a milestone," said Dr. Gupta. "Our aim is to bridge the gap between theoretical knowledge and clinical practice, focusing on how technological evolution in radiation oncology is directly translating into improved survival and better quality of life for our patients."

The academic sessions centered on the theme of evolving treatment paradigms, with in-depth discussions on advanced radiation techniques like IMRT, as exemplified by landmark clinical trials. The program was designed to be highly interactive, featuring lectures, panel discussions, and case-based presentations to foster a dynamic learning environment for the postgraduate trainees.

The event also highlighted the crucial role of industry-academia collaboration. Sun Pharma was acknowledged for its unwavering and continued support of such academic initiatives. In a special gesture, the leadership of AROI and Sun Pharma felicitated each other, celebrating their long and fruitful association in advancing oncology education in India. Mr. Arvind Suri, General Manager of Sales and Marketing, represented Sun Pharma at the event.

The Chief Guest, the Principal of the Medical College, lauded the organizers for hosting an event of such national importance. "It is a matter of great pride for our institution to host this landmark 50th PG course. We are committed to providing a platform for academic excellence and fostering the skills of the next generation of doctors who will lead the fight against cancer," he stated during his address.

The event concluded with the distribution of certificates, feedback from attendees, and a vote of thanks by the organizing committee.

The course concluded successfully, leaving the 80 attending students enriched with updated knowledge and inspired to incorporate cutting-edge, patient-centric approaches into their future practice. The 50th AROI-ICRO PG Teaching Course stands as a proud milestone, reinforcing the mission to nurture the next generation of oncologists through evidence-based, practice-oriented learning.

Glimpses of 50th AROI ICRO SUN PG Teaching Course

51st AROI ICRO SUN Postgraduate Teaching Programme

The 51st AROI SUN Postgraduate Teaching Program was successfully conducted on the 11th and 12th of October, 2025 at Vydehi Institute of Medical Sciences and Research Centre, Bangalore. The academic event focused on ―Paediatric and Hematological malignancies‖ and was organized by the Department of Radiation Oncology.

The program was formally inaugurated by AROI President Prof.(Dr). S. N. Senapati, AROI Secretary General Dr. Srinivasan, ICRO Secretary Dr. Pooja Nandwani Patel, Principal of VIMS & RC Dr. Shreedhar Venkatesh, and Medical Superintendent Dr. M.Umamaheswar . During the inaugural session, the dignitaries emphasized the significance of gaining in-depth knowledge in paediatric and hematological malignancies as these cancers present unique challenges in diagnosis and treatment .They also stressed the need for such focussed courses to equip the Radiation Oncology residents to manage these complex cases .

The teaching sessions witnessed active participation from more than 80 postgraduate students across the country. Distinguished national faculties delivered comprehensive lectures, resolved participants' queries, and enriched the academic discussions with their expertise. The highlight of the academic event was the panel discussion conducted by Prof.(Dr .)S.N.Senapathi .The entire program was conducted smoothly by Dr.Geeta.S.Narayanan (Program Director) and Dr. Arpitha.S (Organizing Secretary) with maximum attendance on both the days .

The event concluded with a quiz competition, in which Dr Omal Shereef (Mahavir Cancer Sansthan and Research Centre, Patna) and Dr Avilash Banerjee (Yashoda Institute of Cancer Centre, Hyderabad) emerged as winners. Both candidates were awarded a fully sponsored trip to Kolkata to attend the forthcoming AROI Conference. The program concluded with a valedictory session and distribution of certificates.

Glimpses 51st AROI ICRO SUN
Postgraduate Teaching Programme

Congratulations

50th ICRO QUIZ WINNERS

1st Dr R Vinayak Padmanaban
GAAMCH, Kanchipuram

2nd Dr Mayank Soni,
AIIMS Rishikesh

51st AROI SUN QUIZ WINNERS

1st Dr Omal Shereef
2nd year DNB Resident
Mahavir Cancer Sansthan, Patna

2nd Dr Avilash Banerjee
JR3 at Yashoda Super Speciality
Hospital, Hyderabad.

AROICON Madhya Pradesh & Chhattisgarh State Chapter

It is immense pleasure to inform that Regional Cancer Centre Raipur has organized state conference of MP CG Chapter "AROICON MPCG2025" on 5th and 6th September 2025. The theme of the conference was “PRESCISION, PROGRESS & POSSIBILITIES IN ONCOLOGY: PRESENT & FUTURE”
The venue of the conference was Atal Bihari Vajpayee Auditorium, Pt. J.N. M. Medical college Raipur Chhattisgarh. The organizing committee as follows:

Session was started with welcome address by chief patron at 9:30 am on 5th September. The scientific programmed was well framed and divided site wise. It consisted of Oration, Pannel discussion, topics on cancer registry, AI, Immunotherapy, nursing care, hematological malignancies, recent advances and newer techniques in radiation oncology. Dr MS Dwivedi oration was Delivered by Professor Vivek Choudhary, Dean and Director RCC, Pt. J.N.M. Medical College Raipur.
Inauguration done by Honorable Chief Minister of Chhattisgarh Shri Vishnu Dev Sai, Dr Raman Singh, Honorable Speaker of Legislative assembly CG, Mr. Shyam Bihari Jaiswal health minister CG.
Total 31 faculties across India, 30 faculties from medical college, around 200 delegates and 23 persons from trade participated in the conference. 30 students presented their research work as poster and oral presentation. I student from BHU, 1 from Delhi, 1 from Calcutta also presented his research work. Winers of each poster and oral presentation were awarded with medal and price money for 1st, 2nd, and 3rd position.
Among member of National Body Dr. V. Srivinivan, Secretary General Of AROI, graced the occasion with his presence. First day of event was ended with GBM in presence of all the members of chapter, Minutes of which attached for reoffence. Dr. Srinivasan also joined GBM as guest member.

The conference was ended on 6th at 3:00 pm. Everybody appreciated the conference for Scientific content, Venue, team work, coordination and organizing such a big event in very short span of only two months.

Glimpses of AROICON
Madhya Pradesh & Chhattisgarh State Chapter

AROICON Jharkhand State Chapter

Association of Radiation oncologist India (AROI) group of Jharkhand conducted 3rd AROICON 2025 Jharkhand chapter conference successfully on 21 september 2025 at courtyard Marriot kanke road.
There were more than 60 oncologists from the entire Jharkhand and other parts of country Mumbai, delhi, Kolkata and Cuttak to discuss about esophageal cancer, bone and soft tissue sarcoma and Lymphoma.
The conference was done under banner of AROICON Jharkhand chapter with association of Ranchi Cancer Hospital and Research Centre and was organized by state secretary Dr Deepak Kumar and state president Dr Aftab Alam Ansari.
Guest speaker in this conference were Dr Indu Bansal , Paras Hospital Delhi, Dr Jifmi Jose, TMH Mumbai, Dr Vivek Verma, Max Hospital Delhi and Dr Rimpa Achari, TMC Kolkata. Chief guest was Prof SN Senpati from AHRCC, Cuttack. Expert from fields discussed about how to manage difficult cases and impart innovative ideas in cancer care. Dr Vivek Verma discussed about limb salvage surgery, means surgery without losing the limb in sarcoma. Other experts discussed about challenges in cancer management especially in low economic state like Jharkhand and how we to deliver best management with limited resources.
Dr SN Senapati suggestion to develop one cancer centre as centre of excellence in each state and oncologist need to work in unison for this.

Other oncologist who were present and gave their contribuations were Dr Ajay Agrawal, Dr Kumar Saurabh, Dr Amitesh, Dr Gunjesh, Dr Amit, Dr SK kundu, Dr Sneha Jha, Dr Anamika, Dr TM singh, Dr Ajit Kushwaha, Dr Mannavi, Dr Aditya, Dr Abhisekh Verma and others.

Glimpses of AROICON Jharkhand State Chapter

AROICON Bihar State Chapter

The 7th annual conference of AROI Bihar Chapter was held successfully at Hotel Maurya, Patna on 12th and 13th July 2025, organized in association with Paras Hospital, Patna. This beautiful conference was well inaugurated by His excellency Hon' Governor of Bihar Mr. Arif Mohammed Khan. It was well attended by Delegates, Postgraduates and faculties not only from Bihar but also from different states of the country and abroad Nepal and Bangladesh.

The theme of this 7th annual conference was 'From evidence to excellence in oncology- A collaborative approach.' The Whole Scientific program was focusing on recent trends in practice of modern oncology well executed by high quality lectures delivered by renowned speakers from TMH (Mumbai), CMC (Vellore), AIIMS(Delhi), RGCI (Delhi), SGPGI (Lucknow), Max (Delhi), Paras (Gurugram) and other prestigious cancer institutes of the country. For the first time at the regional level, after each keynote lecture, Online quiz competition for postgraduates was held successfully. Best three abstract competition was also held among PGs, Residents and senior residents. Quality of the abstracts had been presented of high standard which were well appreciated by judges. Dr. A.D. Singh oration and Dr. Rangi Prasad Singh oration were held in memory of legendry in the field of Radiation oncology of the country.

The organizing secretary Dr. Shekhar Kumar Keshri welcomed the guest speakers and all delegates to begin the conference and finally, Organizing president Dr. Rajiv Ranjan Prasad had given the vote of thankx to all respected faculty and attendees. It was a well organized collaborative conference by all executives from AROI Bihar justifying the theme a collaborative approach academically too.

The graceful presence and blessings of our AROI National President Dr. S.N. Senapati and Secretary General, National AROI Dr. V. Srinivasan, made this conference a grand success.

Glimpses of AROICON Bihar Chapter

Master Class in Radiobiology – AROI NE Zone, Guwahati.

A highly informative Master Class in Radiobiology was conducted on 7th September, 2025, under the aegis of the Association of Radiation Oncologists of India (AROI) – North East Zone, by Professor Manoj Gupta.

FELLOWSHIP APPLICANTS 2025
45th AROICON AT KOLKATA 2025

A. OVERSEAS FELLOWSHIPS:

Age Group	Names of Applicants
More than 50 Years	Dr. Indu Bansal Aggarwal Dr. Siddanna R. Palled Dr. Simon Pavamani
41 – 50 Years	Dr. Shagun Misra Dr. Monica Malik Dr. M. S. Athiyamaan Dr. Pankaj Kumar Dr. Divya Khosla Dr. Aparna M. P. Dr. Priya Iyer Dr. Kanhu Charan Patro Prof. (Dr.) Kailash Kumar Mittal Dr. Susovan Banerjee Dr. Supriya Mallick Dr. Suparna Kanti Pal Lt. Col. Niharika Bisht
35 – 40 Years	Dr. Ajay Sasidharan Dr. Ayush Garg Dr. Satyajeet Rath Dr. Vengada Krishnan P. R. Dr. Saumyaranjan Mishra Dr. Johan Sunny Kilikunnel Dr. K. Sruthi Dr. Deepak Kumar Dr. Deepika Malik Dr. Shirley Lewis Dr. Tejshri Telkhade Dr. Vishwadeep Mishra Dr. Niketa Thakur

Age Group	Names of Applicants
30 – 35 Years	Dr. Ajitesh Avinash Dr. Abhishek Krishna Dr. Tapas Kumar Dash Dr. Siddhartha Adhikary Dr. Debjit Ghosh Dr. Gautam Vydia Dr. Prarabdh Singh Dr. Pratibha Kole Dr. Rashmi Yadav Dr. Abhinandan Das Dr. Jeevi Selvarajan Dr. Vijayeta Ray Dr. Debanjan Kundu Dr. Shruti Bansal Dr. Janmenjoy Mondal Dr. Abhay Chakravarty Dr. Raka Banerjee Dr. Sujata Sarkar Dr. Shinjini Chakrabarty Dr. Shubham Dokania

Important Events at AROICON 2025

ICRO General Body Meeting

Date: Thursday, 27th November 2025
Venue: Hall B
Time: 17:30 – 18:00 Hrs

AROI Central Executive Committee Meeting

Date: Friday, 28th November 2025
Venue: Hall G
Time: 16:00 – 17:30 Hrs

Annual General Body Meeting

Date: Saturday, 29th November 2025
Venue: Hall A
Time: 18:00 – 19:00 Hrs

B WITHIN INDIA FELLOWSHIPS

a. NEIL JOSEPH FELLOWSHIP

Fellowship Type	Names of Applicants
Neil Joseph Fellowship	Dr Saarthak Miglani Dr Mishar Biswas Dr Vanshika Rastogi Dr Nandita Samanta Dr Kaniz Fatima Dr Kriti Chakrabarty Dr Soumava Mondal Dr Debopam Purakayastha Dr Anjalikrishna N P Dr Rohit Golla Dr Sucheta Das Das Dr Soumya Subhadarsini Dr Amirthvarshan A Dr Avilash Banerjee Dr Subrato Mondal Dr Aryan Malhotra Dr Smriti Ram Dr Anoushka Taneja Dr Parvathi N Dr Dhruv Kumar Mathur Dr Sunav Basu Biswas Dr Prakash Chandra Nayak Dr Pamela Sen Dr Pritha Mondal Dr Arshmeen Kaur Anand Dr Pasuspuleti H H Manikanta Sai Hanuman Dr Salma Shams C Dr Bibekananda Rout Dr Shivananda Jena Dr Urvashi Gupta Dr Kamku Bagang Dr Harpreet Kaur Dr Shounak Jairam Kamat Dr Pranav P V Dr Abhinash Bhuyan Dr Reshma Raghunath Dr Gyani Chandrasekhar Behera Dr Dipanjan Nandi Dr Preeti Kaushal Dr P. Harish Kumar Dr Dhruv Rajiv Kabad Dr Srilekha Balaga Dr Shubham Koirala

Radiation Technologist (<45 Yrs)	**Mr Abhishek Pandey**
Medical Physicist (<40 Yrs)	**Dr Dilson Lobo** **Ms Priyanka Agarwal** **Dr Atul Mishra** **Mr Sumanta Manna**
Best Proffered Paper (>40 Yrs)	**Dr Pankaj Kumar** **Dr Karthika Nageswararaj** **Dr Deepti Sharma** **Dr Ram Madhavan** **Dr Priya Iyer** **Dr Kailash Kumar Mittal** **Dr Dev Kumar Yadav** **Dr Supriya Sastri Chopra** **Dr Suneetha N.**
Proffered Paper (35–40 Yrs)	**Dr Satyajeet Rath** **Dr K. Sruthi** **Dr Shirley Lewis** **Dr Anbarasi K** **Dr Sujata Sarkar** **Dr Abhishek Krishna**
Dr KT Bhowmik Young Doctor Award	**Dr Sujata Sarkar** **Dr Johan Sunny Kilikunnel** **Dr Debanjan Kundu** **Dr Shruti Bansal** **Dr Vasanthapriya Subramani** **Dr Adil Ahmed Khan** **Dr Rishi P. Nair** **Dr Raka Banerjee** **Dr Tapas Kumar Dash** **Dr Sanskriti Poddar** **Dr Anita Priyadarshini** **Dr Tarun Jose** **Dr Sheel Mohanty** **Dr Abhishek Krishna** **Dr Kushal Goswami** **Dr N V S Praveen** **Dr Naziba Karim Khondekar** **Dr Kevin Fernando** **Dr Nagarjuna Burela** **Dr Prabha Verma** **Dr Ajinkya Pankaj Gupte**

Dr M S Gujral / Dr M C Pant Gold Medal	**Dr. Sakshi Garg** **Dr Dhruv Mathur** **Dr Arunima Nagar** **Dr Yamini Bisht** **Dr Saarthak Miglani** **Dr Sucheta Das Das** **Dr Pasuspuleti H H Manikanta Sai Hanuman** **Dr Aryan Malhotra** **Dr Smriti Ram** **Dr Anoushka Taneja** **Dr Sevika N** **Dr Salma Shams C** **Dr Sanjay Arvind Krishna** **Dr Urvashi Gupta** **Dr Nayantara Pitaliya** **Dr Pranav P V** **Dr Shubham Koirala** **Dr Pamela Sen** **Dr Eresh Parashar** **Dr Dakshita Singh** **Dr Sunav Basu Biswas** **Dr Vinayak Padmanabhan** **Dr Parth Chandreshbhai Asodariya** **Dr Souvik Das** **Dr Md Nawaz Sharif** **Dr Kanishka Kakkad** **Dr Mamata Birajdar** **Dr Miranda Thoudam** **Dr Ananya Ghosh** **Dr Moumita Das** **Dr Ankita Kusary** **Dr Rima Karmakar** **Dr Saikat Mondal** **Dr Subham Pal** **Dr Shivangi Agnihotri** **Dr Sahil Shah** **Dr Harismita Devi** **Dr Febina K Naisam** **Dr Apala Bhattacharjee** **Dr Punyasha Mohanty** **Dr Kalyani Prakash** **Dr Arit Bhattacharjee** **Dr Soumya Subhadarsini** **Dr Pratik Manik Arote** **Dr RAVURI KIRANMAYI** **Dr Meghana Mekala** **Dr Mirudhula C R** **Dr Fatema Saifuddin Topiwala** **Dr Pritha Mondal** **Dr Anushiya K**

	Dr Navaneetha Lakshmi R **Dr Padma Priya** **Dr Gayathri Karthikeyan** **Dr Ananya Nandi** **Dr Priyanka Das** **Dr Devashish Watts** **Dr Saloni Arora** **Dr Priyalice Tatapudi**
Gold Medal - Medical Physics	**Dr Ganeshkumar** **Ramesh Patel** **Dr Dilson Lobo** **Ms PriyankaAgarwal** **Dr Atul Mishra** **Mr Ajay Katake** **Mr Sanjib Gayen** **Dr Vysakh** **Raveendran** **Mr Sumeesh S**

Sterling HOSPITALS

GASTRO INTESTINAL ONCOLOGY SOCIETY
GIOS

GIOS

3rd ANNUAL CONFERENCE
GASTRO INTESTINAL ONCOLOGY SOCIETY

(Bridging Practice to Evidence in GI Malignancies)

18–20 September 2026
Ahmedabad

SAVE THE DATE

Managed by:
MIGHTY DUO
Ravindra Purohit
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Sterling HOSPITALS

GASTRO INTESTINAL ONCOLOGY SOCIETY GIOS

Dear Colleagues,

It is with great pleasure that we invite you to the **3rd Annual Conference of the Gastro Intestinal Oncology Society (GIOS),** to be **held from 18 – 20 September 2026 at Ahmedabad.**

Building on the success of our previous meetings, this year's conference will unite leading clinicians, researchers, and academicians to share the latest advances in gastrointestinal oncology. **The conference is proudly hosted by Sterling Hospitals, Gujarat's first corporate hospital, with six centers across the state and over two decades of excellence in patient care.**

The program will feature interactive workshops, evidence-based discussions, and multidisciplinary sessions designed to foster collaboration and innovation in patient care.We look forward to welcoming you to Ahmedabad for three enriching days of learning, networking, and warm hospitality.

Warm regards,

PATRON

Dr. Simmardeep S Gill
MD & CEO,
Sterling Hospitals

ORGANIZING SECRETARY

Dr. Pooja Nandwani Patel
Director - Radiation Oncology
Sterling Hospitals, Ahmedabad

SCIENTIFIC CHAIRS

Dr. Bhavin Shah
Consultant - Medical Oncology
Sterling Hospitals,
Ahmedabad

Dr. Vibha Naik
Director - Medical Oncology &
Bone Marrow Transplant
Sterling Hospitals, Vadodara

GIOS OFFICE BEARERS

Dr. Reena Engineer
President,
GIOS

Dr. Jagdish Kothari
Vice President,
GIOS

Dr. Rahul Krishnatry
Secretary,
GIOS

Dr. Rashi Agarwal
Treasurer,
GIOS

Dr. Sayan Paul
Joint Secretary,
GIOS

Sterling HOSPITALS

GASTRO INTESTINAL ONCOLOGY SOCIETY GIOS

REGISTRATION DETAILS

Registration Period	Faculty & Delegate (Member)	Faculty & Delegate (Non-Member)	Students
Prelaunch Offer (Till 15 November 2025)	₹4,500	₹6,500	₹3,000
Early Bird (Up to 15 August 2026)	₹6,500	₹8,500	₹4,000
Late Registration (From 16 August 2026)	₹8,500	₹10,000	₹5,000

WORKSHOP REGISTRATION

Category	Faculty & Delegate (Member)	Faculty & Delegate (Non-Member)	Students
Workshop Fee	₹1,500	₹1,500	₹1,000

SCAN OR CLICK TO REGISTER

For any queries,
email 3rdgios@gmail.com or
call +91 92892 86611
+91 99985 20100

BECOME GIOS MEMBER

Become a member of the **Gastro Intestinal Oncology Society (GIOS)** and join a network of leading clinicians, scientists, and researchers. Collaborate, share knowledge, and contribute to advancing GI cancer research and patient care. Together, we can shape the future of intestinal oncology

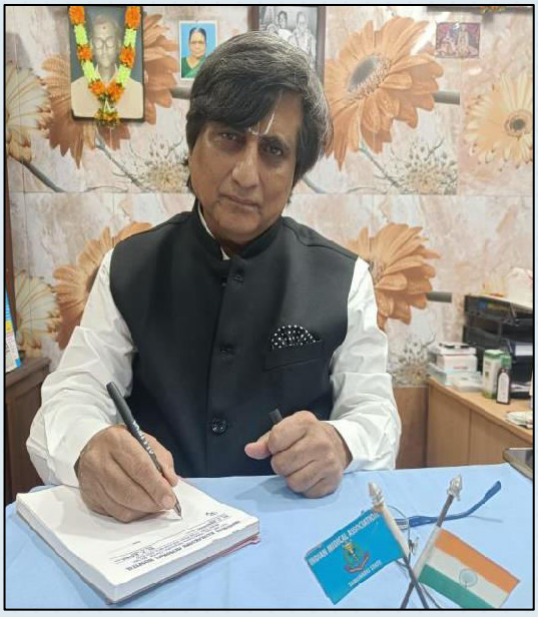
SCAN Or Visit for More Details
https://www.gioncologysociety.com/membership

Date : 27th - 30th November 2025 | Venue : Biswa Bangla Convention Centre, Kolkata, India

Scientific Program Summary

Day	Date	Schedule	Time	Hall A	Hall B	Hall C	Hall D	Hall E	Hall F
Day 1 Thursday	27.11.2025	0930 - 1730	360 mins	-	AROI (ICRO) ASCO Joint Session		-	-	-
		1730 - 1800	30 mins	-	ICRO General Body Meeting		-	-	-
		1800 - 1900	60 mins	Cultural Program (in Hall A)					
Day 2 Friday	28.11.2025	0800 - 0900	60 mins	How I Do It?	How I Do It?	How I Do It?	How I Do It?	How I Do It?	Oral Papers
		0900 - 0930	30 mins	Keynote Lecture	Keynote Lecture	Keynote Lecture	Keynote Lecture	Keynote Lecture	
		0930 - 1230	180 mins	Head and Neck Cancer	Neuro-Oncology	Lung Cancer	GI cancers	Patient Centered Care 1	Miscellaneous Session
		1230 - 1330	60 mins	Dr. B D Gupta Memorial Oration (in Hall A)					
		1330 - 1430	60 mins	Lunch / Poster viewing					
		1430 - 1500	30 mins	Keynote Lecture	Keynote Lecture	Keynote Lecture	Keynote Lecture	Keynote Lecture	Miscellaneous Session
		1500 - 1830	210 mins	Gynecological Cancers	Genitourinary Cancers	Breast Cancer	Muskuloskeletal Cancers	Patient Centered Care 2 Quiz for Residents	
		1900 Onwards		Inauguration and Cultural Program (in Hall A)					
Day 3 Saturday	29.11.2025	0800 - 0900	60 mins	How I Do It?	How I Do It?	How I Do It?	YROF Theme : Education in Oncology		Miscellaneous Session
		0900 - 0930	30 mins	Keynote Lecture	Keynote Lecture	Keynote Lecture			
		0930 - 1130	120 mins	Breast Cancer	Gynaecological Cancers	Head and Neck Cancer		Economics and Practise of Oncology	
		1130 - 1230	60 mins					AROI Proton Therapy Symposium supported by IBA	
		1230 - 1330	60 mins	Padma Shree Dr. Ketayun A Dinshaw Memorial Oration (in Hall A)					
		1330 - 1430	60 mins	Lunch / Poster Viewing					
		1430 - 1500	30 mins	Keynote Lecture	Keynote Lecture	Keynote Lecture	Keynote Lecture		Oral Papers
		1500 - 1630	90 mins	Lung Cancers	GI Cancers	Genitourinary Cancers	Haematolymphoid Cancers	Quality and Safety in Radiotherapy / Personalized Radiotherapy	
		1630- 1800	90 mins	Best Paper Oral Rounds (in Hall A)					
		1800 - 1900	60 mins	Annual General Body Meeting (in Hall A)					
		1900 Onwards		Gala Dinner and Cultural Program (at Mistika Banquet)					
Day 4 Sunday	30.11.2025	0800 - 0900	60 mins	How I Do It?	How I Do It?	How I Do It?	How I Do It?		
		0900 - 0930	30 mins	Keynote Lecture	Keynote Lecture	Keynote Lecture	Keynote Lecture		
		0930 - 1030	60 mins	Padma Shree Dr. M Krishnan Nair Memorial Oration (in Hall A)					
		1030 -1330	180 mins	Neuro-Oncology	Innovations	Paediatric Cancers	AROI AMPI Joint Session	Oral Papers	Miscellaneous Session
		1330 - 1400	30 mins	Valedictory Session					
		1400 - 1500	60 mins	Lunch					

Congratulations



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Congratulations

Congratulations Dr. Ajay G. V.

Assistant Professor
Department of Radiation Oncology
Kidwai Memorial Institute of Oncology

Gold Medal in Table Tennis

He won at the National Para Table Tennis Tournament held in Indore

A moment of immense pride and inspiration!

AROI Bihar Chapter Registered

We are pleased to announce that the Association of Radiation Oncologists of India, Bihar Chapter has been officially registered on 4th September 2025 under the Societies Registration Act, 1860 (Act No. XXI), vide Registration No. S000221 (Year 2025–2026).

Official Website: www.aroi-bih.org
Email : aroibiharchapter@gmail.com

Obituary

We deeply mourn the passing of Dr. Jayashankar Raju, Consultant Radiation Oncologist, on 11th September 2025, at the age of 71 years.

He was from the first batch of Postgraduates of Kidwai Memorial Institute of Oncology and dedicated his life to the service of cancer patients. May his soul rest in peace.

Students Corner

Neuroendocrine Neoplasm

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Section 1. Introduction and Historical Perspective

1.1 Historical Evolution

- **1907 – Oberndorfer's "Karzinoide":** Small bowel tumors with carcinoma-like appearance but slow growth were described as ―carcinoid,‖ thought benign.
- **Mid-20th century:** Recognition of malignant potential as many showed nodal/liver metastases.
- **1950s–60s:** Discovery of serotonin secretion and its metabolite (5-HIAA) explained **carcinoid syndrome**.
- **1970s–80s:** IHC tools (chromogranin A, synaptophysin) allowed reproducible diagnosis.
- **1990s:** Imaging and functional tracers (^111In-pentetreotide, Octreoscan) enabled systemic staging.
- **2000s:** WHO classification + ENETS staging standardized global practice; Ki-67 introduced as grading index.
- **2010s:** SSAs proven antiproliferative (PROMID, CLARINET), targeted therapies (everolimus, sunitinib), PRRT validated (NETTER-1).
- **2020s:** NETTER-2 moved PRRT earlier in G2–G3; CABINET trial introduced cabozantinib. WHO refined **NET G3 distinct from NEC**.

1.2 Why Important

- **Rising incidence:** From ~1/100,000 (1970s) → >7/100,000 today.
- **High prevalence:** Due to long survival even with metastases.
- **Heterogeneity:** NET G1 indolent, NEC highly aggressive.
- **Functional syndromes:** Unique to NENs, requiring endocrine + oncologic management.
- **Model for theranostics:** NETs are the prototype for diagnostic–therapeutic pairing (^68Ga-DOTATATE PET → ^177Lu-PRRT).
- **Multidisciplinary care:** Requires integration of surgery, oncology, endocrinology, nuclear medicine, pathology, cardiology.

1.3 Learning Objectives

- Understand classification evolution.
- Recognize heterogeneity (NET vs NEC, G1–G3).
- Know why NETs are rising in incidence and clinical significance.
- Learn their role as **teaching model for precision oncology**.

Section 2. Classification and Taxonomy

2.1 WHO 2022/24 Framework

- **Neuroendocrine Tumors (NETs, well-differentiated):**
  - NET G1, G2, G3 (graded by Ki-67 and mitoses).
- **Neuroendocrine Carcinomas (NECs, poorly differentiated):**
  - Small cell and large cell types; always high-grade.
- **Mixed Neuroendocrine–Non-neuroendocrine Neoplasms (MiNENs):**
  - Each component ≥30%.

2.2 Grading

- **G1:** Ki-67 ≤2–3%, <2 mitoses/2 mm².
- **G2:** Ki-67 3–20% or 2–20 mitoses/2 mm².
- **G3:** Ki-67 >20% or >20 mitoses/2 mm² *with well-diff morphology*.
- **NEC:** morphology-driven (p53 abnormal, Rb loss), often Ki-67 >55%.
- **Rule:** when Ki-67 and mitoses differ, assign **higher grade**.

2.3 Site-Specific Variations

- **GEP-NETs:** use full grading (G1–G3).
- **Lung NETs:** classified as typical carcinoid, atypical carcinoid, LCNEC, SCNEC — based on mitoses + necrosis (not Ki-67).
- **Merkel cell carcinoma:** cutaneous NEC, CK20+ dot pattern, often polyomavirus-driven.

2.4 Functional vs Non-Functional

- **Functional NETs:** clinically active (carcinoid syndrome, insulinoma, gastrinoma, VIPoma, glucagonoma, somatostatinoma).
- **Non-functional NETs:** majority of pancreatic NETs; often incidental detection.

2.5 Genetic Syndromes

- **MEN1:** pNETs, pituitary, parathyroid.
- **VHL:** pNETs, RCC, hemangioblastomas.
- **NF1:** duodenal somatostatinoma.
- **TSC:** rare pNETs.
- **RET (MEN2):** medullary thyroid carcinoma.
- **SDHx:** paragangliomas, pheochromocytomas.

2.6 Exam Pearls

- **Primary axis:** differentiation (NET vs NEC).
- **Secondary axis:** grade (G1–G3).
- **NET G3 ≠ NEC.**
- **MiNEN:** both components ≥30%.
- **Lung NETs:** graded differently (mitoses/necrosis, not Ki-67).

Section 3. Epidemiology and Natural History

3.1 Incidence & Prevalence

- Rising incidence (SEER: ~7-fold increase).
- NETs now 2nd most prevalent GI cancer after CRC.
- High prevalence due to long survival even in metastatic disease.

3.2 Distribution

- Small intestine (30%), rectum (20%), pancreas (15%), stomach (7%), colon/appendix (10%), lung (20%).
- Rectal NETs more frequent in Asia; small bowel NETs in Western cohorts.

3.3 Demographics

- Median age: ~60 yrs.
- Earlier onset in syndromic NETs.
- Slight female predominance overall.

3.4 Indian Data

- More rectal/pancreatic NETs, younger presentation.
- Limited PRRT access.
- Increasing incidental detection via endoscopy.

3.5 Natural History

- **NET G1/G2:** indolent, survival often >7–10 yrs metastatic.
- **NET G3:** intermediate, median OS ~2–4 yrs.
- **NEC:** highly aggressive, median OS <1 yr.

3.6 Prognostic Factors

- Grade (Ki-67, mitoses).
- Stage (TNM, liver burden).
- Primary site (ileal better, colon worse).
- Differentiation (NET vs NEC).
- Imaging phenotype (SSTR+ vs FDG+).
- Functional status (hormone syndromes).

3.7 Outcomes

- Localized NET: 5-yr OS >90%.
- Regional: 70–80%.
- Distant: NET G1/2 → 40–60%, NET G3 → 20–30%, NEC → <15%.

3.8 Key Exam Points

- Incidence rising sharply due to detection.
- Survival strongly grade- and site-dependent.
- Small bowel NET → best long-term outcomes; colonic NEC → worst.

Section 4. Pathology and Immunohistochemistry of Neuroendocrine Neoplasms (NENs)

4.1 General Principles

Neuroendocrine neoplasms (NENs) are **epithelial tumors** that demonstrate:

- **Morphological neuroendocrine differentiation** (organoid patterns, stippled nuclei).
- **Expression of neuroendocrine markers** on immunohistochemistry (IHC).

Pathology is pivotal in NEN diagnosis and management because **clinical outcomes and treatment selection** depend on two critical parameters:

1. **Differentiation** – whether a tumor is a **well-differentiated neuroendocrine tumor (NET)** or a **poorly differentiated neuroendocrine carcinoma (NEC)**.
2. **Grade** – proliferation rate measured by **mitotic count** and **Ki-67 labeling index**.

Modern classification integrates:

- Light microscopic morphology.
- Proliferation indices (mitotic activity and Ki-67).
- IHC markers (synaptophysin, chromogranin A, insulinoma-associated protein 1 [INSM1], etc.).
- Molecular alterations (multiple endocrine neoplasia type 1 [MEN1], alpha thalassemia/mental retardation syndrome X-linked [ATRX], death-domain associated protein [DAXX], tumor protein p53 [TP53], retinoblastoma gene [RB1]).

4.2 Morphology

A. Well-Differentiated Neuroendocrine Tumor (NET)

- **Architecture:** Organoid nests, trabecular ribbons, acinar patterns, or rosettes.
- **Cytology:** Uniform cells with moderate cytoplasm, finely stippled ―salt-and-pepper‖ chromatin, inconspicuous nucleoli.
- **Mitotic activity:** Rare in Grade 1 (G1); progressively higher in Grade 2 (G2) and Grade 3 (G3).
- **Necrosis:** Absent or focal punctate in higher grades.
- **Stroma:** Richly vascularized; may show hyalinization.

B. Poorly Differentiated Neuroendocrine Carcinoma (NEC)

Two morphologic subtypes:

1. **Small Cell NEC (SCNEC):** Resembles small cell lung carcinoma. Features include small cells, high nuclear-to-cytoplasmic ratio, hyperchromatic nuclei, nuclear molding, brisk mitoses (>20–40 per 2 mm^2), and extensive necrosis.
2. **Large Cell NEC (LCNEC):** Composed of large polygonal cells with abundant cytoplasm, vesicular nuclei, prominent nucleoli, frequent mitoses, and geographic necrosis.

Key Clinical Note: Morphology **supersedes proliferation index**. For example, a tumor with Ki-67 ~30% but classical NEC morphology must be reported as NEC, not NET Grade 3.

4.3 Grading Criteria (World Health Organization 2022/2024 for Gastroenteropancreatic NETs)

- **Grade 1 (G1):** Mitotic count <2 per 2 mm²; Ki-67 ≤2–3%.
- **Grade 2 (G2):** Mitotic count 2–20 per 2 mm² or Ki-67 3–20%.
- **Grade 3 (G3):** Mitotic count >20 per 2 mm² or Ki-67 >20% **with well-differentiated morphology**.

Important Notes:

- In case of discrepancy between mitotic count and Ki-67, the **higher grade prevails**.
- At least **500–2000 tumor cells** should be counted in a hotspot for Ki-67 index determination.
- Inter-observer variability exists; method of assessment (manual vs digital) must be documented.

Exam Pearl: *NET Grade 3 (well-differentiated, high Ki-67) is biologically distinct from NEC (poorly differentiated). Immunostains for p53 and Rb help separate the two entities.*

4.4 Immunohistochemistry (IHC)

A. Diagnostic Neuroendocrine Markers

- **Synaptophysin:** Most sensitive, diffusely positive in both NET and NEC.
- **Chromogranin A:** More specific, strong in NET but often weak/patchy in NEC.
- **Insulinoma-associated protein 1 (INSM1):** Nuclear transcription factor, highly sensitive and specific for neuroendocrine differentiation.
- **Cluster of differentiation 56 (CD56):** Sensitive but nonspecific (positive in lymphomas, sarcomas).

B. Lineage and Site Identification Markers

- **Cytokeratin 7 (CK7)/Cytokeratin 20 (CK20):** Helps differentiate intestinal vs pancreatic origin.
- **Thyroid transcription factor-1 (TTF-1):** Positive in pulmonary NETs/NECs.
- **Paired box gene 8 (PAX8):** Suggests pancreatic, thyroid, or renal origin.
- **Caudal type homeobox 2 (CDX2):** Indicates intestinal origin.

C. Proliferative Marker

- **Ki-67 (MIB-1 antibody):** Mandatory for grading. Report as an exact percentage, not a range.

D. Molecular Surrogates

- **Tumor protein p53 (TP53):**
  - Wild-type (normal expression) in NET.
  - Abnormal (diffuse overexpression or null pattern) in NEC.
- **Retinoblastoma protein (Rb):**
  - Intact in NET.
  - Lost in NEC.
- **Alpha thalassemia/mental retardation syndrome X-linked (ATRX) and Death-domain associated protein (DAXX):**
  - Loss seen in ~40% pancreatic NETs.
  - Associated with alternative lengthening of telomeres (ALT) pathway.

E. Predictive Marker

- **Somatostatin receptor 2A (SSTR2A):**
  - Strong membranous positivity correlates with ^68Ga-DOTATATE uptake.
  - Predicts suitability for peptide receptor radionuclide therapy (PRRT) with Lutetium-177 (^177Lu).

4.5 Molecular Pathology

- **Pancreatic NETs:** MEN1 mutations (~40%), ATRX/DAXX loss (~40%), mammalian target of rapamycin (mTOR) pathway alterations (~15%). These tumors show chromosomal stability and low tumor mutational burden.
- **Midgut NETs:** Generally genetically bland, with occasional alterations in cyclin-dependent kinase inhibitor 1B (CDKN1B).
- **Neuroendocrine Carcinomas (NECs):** Genetically similar to small cell lung carcinoma. Common alterations include TP53 mutations (~90%), RB1 loss (~80%), and MYC amplification.
- **Clinical Impact:**
  - NETs → candidates for somatostatin analogues (SSAs), PRRT, targeted therapies.
  - NECs → chemosensitive to platinum–etoposide regimens, poor PRRT candidates.

4.6 Differential Diagnosis

- **Adenocarcinoma with focal neuroendocrine differentiation:** May express synaptophysin focally but lacks diffuse staining and neuroendocrine morphology.
- **Lymphoma:** Can mimic small cell NEC; lymphoid marker (leukocyte common antigen [LCA]) positive, neuroendocrine markers negative.
- **Merkel Cell Carcinoma vs Metastatic NEC:** Merkel cell is CK20+ with dot-like perinuclear staining, often polyomavirus-associated; metastatic NEC may be TTF-1 positive.

4.7 Pathology Reporting Checklist

Pathology reports should include:

1. Specimen type (biopsy vs resection).
2. Site and size of tumor.
3. Histological type: NET (well-differentiated) vs NEC (poorly differentiated).
4. Grade: mitotic count, Ki-67 index, necrosis.
5. Resection margins.
6. Lymphovascular invasion (LVI) and perineural invasion (PNI).
7. Lymph node status (number examined and involved).
8. IHC profile: synaptophysin, chromogranin A, INSM1, Ki-67, SSTR2A, p53, Rb.
9. Molecular findings if available (MEN1, ATRX, DAXX, TP53, RB1).
10. **Final integrated diagnostic statement.**

Example:—Well-differentiated pancreatic neuroendocrine tumor, Grade 2 (Ki-67 12%, mitoses 4/2 mm²), 3.2 cm, confined to pancreas, lymphovascular invasion present, 2/10 lymph nodes involved, margins free, ATRX loss by IHC, SSTR2A strong membranous positivity.‖

4.8 Clinical Relevance

- **Grade and differentiation** guide systemic therapy (SSA/PRRT for NETs, chemotherapy for NECs)

- **Molecular alterations** help refine prognosis (ATRX/DAXX loss = indolent; TP53/Rb loss = aggressive).
- **SSTR2A expression** predicts PRRT benefit.

4.9 Teaching Pearls (Exam-Oriented)

- Always report both mitotic count and Ki-67.
- NET Grade 3 ≠ NEC; confirm with morphology and p53/Rb status.
- Synaptophysin is more sensitive; chromogranin A is more specific.
- SSTR2A positivity correlates with DOTATATE uptake.
- Mixed neuroendocrine–non-neuroendocrine neoplasms (MiNENs): ≥30% of each component.

Section 5. Staging of Neuroendocrine Neoplasms (NENs)

5.1 Importance of Staging

- Staging provides a **uniform framework** to describe tumor extent, prognosis, and guide treatment.
- Two major systems are in use:
    - **ENETS (European Neuroendocrine Tumor Society):** introduced between 2006–2010, site-specific, widely used in Europe.
    - **AJCC (American Joint Committee on Cancer) 8th edition, 2017/2020 update:** harmonized with ENETS in most sites, globally accepted.

Key Point:

- Both systems are **anatomical TNM-based** (Tumor–Node–Metastasis).
- Differentiation and grade (G1–G3, NET vs NEC) are **reported separately**, not as part of TNM.

5.2 General Rules

- **T (Tumor):** size and depth of invasion.
- **N (Nodes):** regional lymph node involvement.
- **M (Metastasis):** distant spread, especially to liver, bone, or lung.
- **Stage grouping (I–IV):** combines TNM.
- **Grading:** always reported in parallel (Ki-67, mitotic rate).

5.3 Staging by Site

A. Gastric Neuroendocrine Tumors (NETs)

(Based on AJCC 8th edition, harmonized with ENETS)

T Stage	Definition
T1	Invades lamina propria or submucosa, ≤2 cm
T2	Invades muscularis propria or >2 cm
T3	Invades subserosa
T4	Invades serosa or adjacent structures

- **N1:** Regional lymph node metastasis.
- **M1:** Distant metastasis.

Stage grouping:

- I (T1 N0 M0) → Excellent prognosis.
- IV (Any T, Any N, M1) → Poor prognosis.

B. Small Intestinal NETs (Duodenum, Jejunum, Ileum)

T Stage	Definition
T1	≤1 cm, invades lamina propria or submucosa
T2	>1–2 cm, invades muscularis propria
T3	>2 cm or invades subserosa
T4	Invades visceral peritoneum or adjacent organs

- **N1:** Regional lymph nodes involved.
- **M1:** Distant metastases (commonly liver).

Clinical Note:

- Multifocality is frequent (20–25%).
- Mesenteric fibrosis may cause obstruction even with small primaries.

C. Appendix NETs

T Stage	Definition
T1	≤2 cm, limited to appendix
T2	>2–4 cm, limited to appendix
T3	>4 cm or invades ileum/cecum
T4	Invades peritoneum or other adjacent organs

- **N1:** Nodal involvement.
- **M1:** Distant spread (rare).

Special surgical rules:

- <1 cm at tip → appendectomy sufficient.
- 1–2 cm with high-risk features → consider right hemicolectomy.
- 2 cm → right hemicolectomy.

D. Colorectal NETs (Rectum/Colon)

T Stage	Definition
T1	Invades lamina propria or submucosa, ≤2 cm
T2	Invades muscularis propria, >2 cm
T3	Invades through muscularis into subserosa
T4	Invades peritoneum or adjacent organs

- **N1:** Regional node involvement.
- **M1:** Distant metastasis.

Clinical Note:

- Rectal NET ≤10 mm (Grade 1): cured by local excision.
- Rectal NET >20 mm: require radical surgery.
- 10–20 mm: gray zone, decision depends on grade, depth, and lymphovascular invasion.

E. Pancreatic NETs (pNETs)

T Stage	Definition
T1	≤2 cm, limited to pancreas
T2	>2–4 cm, limited to pancreas
T3	>4 cm or invades duodenum/bile duct
T4	Invades celiac axis or superior mesenteric artery (unresectable)

- **N1:** Regional node positive.
- **M1:** Distant metastasis (commonly liver, bone).

Clinical Note:

- For tumors ≤2 cm, active surveillance may be appropriate in select non-functional pNETs.
- Surgical decisions vary with functionality and genetic background (e.g., MEN1).

F. Pulmonary NETs (Lung and Bronchus)

(AJCC 8th edition, same as non-small cell lung cancer staging)

- **Typical Carcinoid (TC):** <2 mitoses/2 mm², no necrosis.
- **Atypical Carcinoid (AC):** 2–10 mitoses/2 mm² and/or necrosis.
- **Large Cell NEC (LCNEC)** and **Small Cell NEC (SCNEC):** high mitoses, necrosis, aggressive course.

T staging parallels non-small cell lung cancer:

- T1 (≤3 cm), T2 (3–5 cm), T3 (5–7 cm), T4 (>7 cm or invasion of mediastinal structures).
- N staging: N0–N3 (ipsilateral, contralateral, mediastinal nodes).
- M staging: M1a (pleural), M1b (single extrathoracic), M1c (multiple).

Clinical Note:

- Pulmonary carcinoids have much better prognosis than LCNEC/SCNEC, even with nodal disease.

5.4 Clinical Staging Investigations

- **Cross-sectional imaging:** Triphasic CT, MRI.
- **Functional imaging:**
  - ^68Ga-DOTATATE PET/CT for well-differentiated NETs.
  - ^18F-FDG (fluorodeoxyglucose) PET/CT for NEC and NET Grade 3.
- **Endoscopic ultrasound (EUS):** Pancreatic and rectal NETs.
- **Intraoperative palpation:** Small bowel NETs (due to multifocality).

5.5 Teaching Pearls (Exam/Clinical)

- Always stage **site-specifically** (pancreas ≠ rectum ≠ appendix).
- **Grade (Ki-67, mitoses)** is not part of TNM, but must always accompany stage.
- **Rectal NETs:** ≤10 mm → EMR/ESD (endoscopic); >20 mm → oncologic resection.
- **Pancreatic NETs:** staging mirrors adenocarcinoma, but biology is distinct.
- **Pulmonary NETs:** staged like lung cancer, but clinical course is far more indolent in carcinoids.
- **AJCC vs ENETS:** broadly harmonized; small variations in definitions, but both widely accepted.

Section 6. Diagnostic Work-Up of Neuroendocrine Neoplasms (NENs)

6.1 Objectives of Diagnostic Work-Up

The goals of the initial evaluation are:

1. Establish **diagnosis** and confirm neuroendocrine differentiation.
2. Determine **site of origin** and **extent of disease** (staging).
3. Assess **functionality** (hormone secretion).
4. Evaluate **tumor biology** (well-differentiated NET vs poorly differentiated NEC).
5. Identify **therapeutic targets** (somatostatin receptor expression, PRRT eligibility).
6. Detect **hereditary syndromes** (MEN1, VHL, NF1, TSC).

6.2 Imaging

A. Cross-Sectional Imaging

- **Computed Tomography (CT):**
  - *Triphasic CT (arterial, portal venous, delayed phases)* is preferred.
  - NETs are typically **hypervascular**, showing arterial phase enhancement.
  - Helpful for detecting primary tumor, liver metastases, mesenteric masses.
- **Magnetic Resonance Imaging (MRI):**
  - Especially useful for **liver metastases** (more sensitive than CT).
  - Diffusion-weighted imaging (DWI) and hepatobiliary contrast agents increase sensitivity.
  - Preferred in younger patients and for long-term follow-up (radiation sparing).

B. Functional Nuclear Imaging

- **Gallium-68 DOTATATE Positron Emission Tomography/Computed Tomography (^68Ga-DOTATATE PET/CT):**
  - Gold standard for well-differentiated NETs.
  - Binds somatostatin receptor subtype 2 (SSTR2).
  - Superior sensitivity to older Octreoscan (^111In-pentetreotide).
  - Detects primary tumors, small metastases, multifocal disease.
  - Guides peptide receptor radionuclide therapy (PRRT).
- **Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography (^18F-FDG PET/CT):**
  - Indicates tumor aggressiveness.
  - High uptake in NEC and NET Grade 3.
  - Often discordant with DOTATATE; dual-tracer imaging stratifies prognosis.
  - **Dual phenotype:**
    - DOTATATE+ / FDG– = indolent NET (good PRRT candidate).
    - DOTATATE+ / FDG+ = heterogeneous NET G2/G3 (consider PRRT + chemotherapy).
    - DOTATATE– / FDG+ = NEC (platinum chemotherapy preferred).

C. Endoscopic Imaging

- **Endoscopic Ultrasound (EUS):**
  - High resolution for small lesions in pancreas and rectum.
  - Enables fine needle aspiration (FNA) or biopsy.
- **Colonoscopy/Upper GI endoscopy:**
  - Detects incidental rectal and gastric NETs.

D. Intraoperative and Other Modalities

- **Intraoperative palpation:** Mandatory in small bowel NETs due to multifocality.
- **Bone scan:** Rarely needed now; replaced by DOTATATE PET.

6.3 Biochemical Testing

A. General Markers

- **Chromogranin A (CgA):**
  - Widely used but nonspecific.
  - Elevated in most NETs, correlates with tumor burden.
  - False positives with proton pump inhibitors (PPIs), chronic atrophic gastritis, renal failure.
- **Pancreastatin:** Fragment of chromogranin A, less influenced by PPIs, more specific.

B. Syndrome-Specific Markers

- **Carcinoid syndrome:**
  - 24-hour urinary 5-hydroxyindoleacetic acid (5-HIAA), end product of serotonin metabolism.
  - Correlates with symptom severity and risk of carcinoid heart disease.

- **Insulinoma:**
  - Fasting test: inappropriately high insulin, C-peptide, and proinsulin with hypoglycemia.
- **Gastrinoma (Zollinger–Ellison syndrome):**
  - Fasting serum gastrin >1000 pg/mL with gastric pH <2.
  - If equivocal: secretin stimulation test (paradoxical rise in gastrin).
- **VIPoma (Vasoactive Intestinal Peptide tumor):**
  - Serum VIP >75 pg/mL; associated with watery diarrhea, hypokalemia, achlorhydria (WDHA syndrome).
- **Glucagonoma:**
  - Elevated serum glucagon >500 pg/mL; presents with necrolytic migratory erythema, diabetes, anemia.
- **Somatostatinoma:**
  - Elevated somatostatin; associated with diabetes, gallstones, steatorrhea.

C. Other Laboratory Tests

- Electrolytes, glucose, and renal/liver function tests.
- NT-proBNP and echocardiography for carcinoid heart disease surveillance.

6.4 Genetic Evaluation

Hereditary syndromes account for ~5–10% of NENs.

- **Multiple Endocrine Neoplasia type 1 (MEN1):** Screen if multiple pancreatic NETs, family history, or age <40.
- **Von Hippel–Lindau (VHL):** Consider if renal cell carcinoma, CNS hemangioblastoma, or pancreatic NET.
- **Neurofibromatosis type 1 (NF1):** Associated with duodenal somatostatinoma.
- **Tuberous Sclerosis Complex (TSC):** Rare pancreatic NETs.
- **RET proto-oncogene mutations:** Medullary thyroid carcinoma.
- **Succinate dehydrogenase (SDHx) mutations:** Paragangliomas, pheochromocytomas.

6.5 Integrative Diagnostic Approach

1. **Initial suspicion**: Incidental imaging finding, symptoms of hormone excess, or mass lesion.
2. **Baseline investigations:**
   - Triphasic CT or MRI (local and metastatic staging).
   - Biochemistry: chromogranin A, syndrome-specific hormones.
3. **Confirm neuroendocrine nature:** Biopsy + IHC (synaptophysin, chromogranin, INSM1, Ki-67).
4. **Determine biology:** DOTATATE PET for NET, FDG PET for NEC/NET G3.
5. **Assess functionality:** Carcinoid, insulinoma, gastrinoma, VIPoma, glucagonoma, somatostatinoma work-up.
6. **Evaluate hereditary syndromes** if indicated (family history, young age, multiple primaries).

6.6 Teaching Pearls

- **DOTATATE PET** is superior to Octreoscan; now gold standard for NETs.
- **FDG PET** is essential in NEC and NET Grade 3; dual-tracer imaging stratifies therapy.
- **Chromogranin A** is widely used but nonspecific; always interpret with clinical context.
- **Rectal and gastric NETs** are often incidental on endoscopy.
- **Pancreatic NETs:** Endoscopic ultrasound with biopsy is diagnostic gold standard.

- **Carcinoid syndrome:** 24-hour urinary 5-HIAA is confirmatory.
- Always distinguish **sporadic vs syndromic NETs** (MEN1, VHL, NF1, TSC).

Section 7. Site-Specific Neuroendocrine Tumors (NETs)

7.1 Gastric Neuroendocrine Tumors (G-NETs)

Subtypes (Rindi classification):

1. **Type 1:**
   - Background: chronic atrophic gastritis → hypergastrinemia → enterochromaffin-like (ECL) cell hyperplasia.
   - Small, multiple, usually ≤1 cm.
   - Indolent, rarely metastasize.
   - Management: endoscopic resection, surveillance; antrectomy in recurrent disease.
2. **Type 2:**
   - Associated with Multiple Endocrine Neoplasia type 1 (MEN1) and Zollinger–Ellison syndrome (gastrinoma).
   - Multiple, small, gastric body lesions.
   - Management: treat gastrinoma; endoscopic resection if localized.
3. **Type 3 (sporadic):**
   - Solitary, often >2 cm, high-grade potential.
   - Aggressive, metastasis risk high.
   - Management: oncologic gastrectomy with lymphadenectomy.

Exam Pearl: Type 1 and 2 → indolent, surveillance feasible. Type 3 → aggressive, always surgical.

7.2 Small Intestinal NETs (SI-NETs; Jejunal/Ileal)

- Most common site in Western populations.
- Frequently **multifocal** (20–25%).
- **Clinical features:** abdominal pain, obstruction, mesenteric mass with desmoplastic reaction, ischemia.
- **Carcinoid syndrome:** flushing, diarrhea, bronchospasm, right-sided heart disease (usually with liver metastases).
- **Surgery:** segmental resection + mesenteric node dissection; intraoperative palpation essential.
- **Systemic therapy:** somatostatin analogues (SSAs), peptide receptor radionuclide therapy (PRRT), targeted agents (everolimus, cabozantinib).

Key Point: Even small tumors can metastasize.

7.3 Pancreatic Neuroendocrine Tumors (pNETs)

Functional vs Non-Functional:

- **Functional pNETs:** produce hormones → specific clinical syndromes.
  - *Insulinoma:* most common; hypoglycemia, usually benign.
  - *Gastrinoma:* causes Zollinger–Ellison syndrome; multiple in MEN1.
  - *VIPoma:* watery diarrhea, hypokalemia, achlorhydria (WDHA).
  - *Glucagonoma:* necrolytic migratory erythema, diabetes, anemia.
  - *Somatostatinoma:* steatorrhea, gallstones, diabetes.
- **Non-functional pNETs:** majority today; discovered incidentally; often larger and metastatic at presentation.

Management:

- **Surgery:** enucleation for small, localized; pancreatectomy for larger/complex.
- **Medical:** SSA for functional tumors and for antiproliferative effect.
- **Advanced disease:** PRRT, everolimus, sunitinib, chemotherapy (CAPTEM regimen).

Exam Pearl: Functional → present earlier, smaller. Non-functional → later, larger, metastatic.

7.4 Appendiceal NETs

- Common incidental finding post-appendectomy.
- **Management depends on size and risk features:**
  - <1 cm at tip: appendectomy sufficient.
  - 1–2 cm: consider right hemicolectomy if base involvement, mesoappendiceal invasion >3 mm, lymphovascular invasion, or high grade.
  - 2 cm: right hemicolectomy.
- Prognosis excellent in most cases.

7.5 Colorectal NETs

Rectal NETs

- Increasingly detected due to colonoscopy.
- **Management by size:**
  - ≤1 cm, Grade 1: Endoscopic resection (EMR/ESD).
  - 1–2 cm: Local excision (endoscopic or transanal) if low grade.
  - 2 cm or high-risk: Radical resection with lymphadenectomy.
- Prognosis: small lesions excellent (>90% cure), larger tumors higher metastatic risk.

Colonic NETs

- Rare, usually right colon.
- Larger, aggressive, poor prognosis.
- Managed like adenocarcinoma → colectomy with nodes.

Exam Pearl: Rectal NET ≤10 mm → local resection curative; colonic NETs behave aggressively.

7.6 Pulmonary NETs (Lung)

Subtypes:

1. **Typical carcinoid (TC):**
   - <2 mitoses/2 mm², no necrosis.
   - Indolent; 5-year survival >90%.
2. **Atypical carcinoid (AC):**
   - 2–10 mitoses/2 mm², necrosis present.
   - More aggressive; nodal metastases common.

3. **Large Cell NEC (LCNEC):**
   - High-grade, large polygonal cells, frequent necrosis.
   - Resembles poorly differentiated carcinoma.
4. **Small Cell NEC (SCNEC):**
   - Classic small cell morphology, aggressive, rapid metastasis.

Management:

- **TC/AC:** surgical resection with systematic nodal dissection. Sleeve resection preferred to preserve lung function.
- **LCNEC/SCNEC:** managed similar to small cell lung carcinoma (platinum-based chemotherapy ± radiation).

Exam Pearl: Pulmonary carcinoids (TC, AC) are biologically distinct from NECs; staging mirrors lung cancer TNM but outcomes are better for carcinoids.

7.7 Clinical Summary Table

Site	Unique Features	Management
Stomach	Type 1 & 2 indolent, Type 3 aggressive	Endoscopic resection vs gastrectomy
Small intestine	Multifocal, mesenteric fibrosis, carcinoid syndrome	Surgery + SSA ± PRRT
Pancreas	Functional vs non-functional, MEN1	Surgery ± SSA, PRRT, targeted therapy, chemo
Appendix	Incidental, size-based management	Appendectomy vs right hemicolectomy
Rectum	Small incidental; size-based prognosis	Endoscopic vs radical resection
Colon	Large, aggressive	Colectomy, poor prognosis
Lung	TC/AC (carcinoid), LCNEC/SCNEC aggressive	Surgery for carcinoid, chemo for NEC

7.8 Teaching Pearls

- **Gastric NET Type 1 and 2** → indolent; **Type 3** → aggressive, always surgical.
- **Small bowel NETs** → multifocal, mesenteric fibrosis; intraoperative palpation essential.
- **Pancreatic NETs:** Functional → earlier, smaller; non-functional → later, metastatic.
- **Appendiceal NETs:** Size and base involvement dictate appendectomy vs hemicolectomy.
- **Rectal NETs:** ≤10 mm → endoscopic cure; >20 mm → radical surgery.
- **Pulmonary NETs:** Carcinoids have excellent prognosis; NECs aggressive like small cell lung carcinoma.

Section 8. Systemic Therapy for Well-Differentiated Neuroendocrine Tumors (NETs)

8.1 Overview

Systemic therapy in well-differentiated NETs (Grades 1–2 and some Grade 3) is guided by:

- **Somatostatin receptor expression (SSTR2A positivity).**
- **Tumor grade and proliferation index (Ki-67).**
- **Symptomatic hormonal activity.**
- **Tumor burden and pace of progression.**

Main systemic options include:

1. Somatostatin analogues (SSAs).
2. Peptide receptor radionuclide therapy (PRRT).
3. Targeted therapy (mTOR and tyrosine kinase inhibitors).
4. Cytotoxic chemotherapy (for selected patients).
5. Liver-directed therapies for hepatic metastases.

8.2 Somatostatin Analogues (SSAs)

Mechanism:

- Bind somatostatin receptor subtype 2 (SSTR2) → inhibit hormone secretion and slow tumor proliferation.

Agents:

- **Octreotide long-acting repeatable (LAR):** 20–30 mg intramuscularly every 4 weeks.
- **Lanreotideautogel:** 120 mg deep subcutaneous every 4 weeks.

Key Trials:

- **PROMID (2009):** Octreotide LAR prolonged progression-free survival (PFS) in midgut NETs.
- **CLARINET (2014):** Lanreotide improved PFS in non-functional gastrointestinal and pancreatic NETs.

Indications:

- First-line therapy in SSTR-positive Grade 1–2 NETs.
- Symptom control in carcinoid syndrome, gastrinoma, VIPoma, glucagonoma.

Toxicities:

- Gallstones, steatorrhea, mild hyperglycemia, abdominal discomfort.

Exam Pearl: SSAs provide both **symptom relief** and **antiproliferative effect**.

8.3 Peptide Receptor Radionuclide Therapy (PRRT)

Concept:

- Delivers targeted radiation by binding radiolabeled SSA to SSTR-positive tumors.
- Standard agent: **Lutetium-177 (^177Lu)-DOTATATE**.

Key Trials:

- **NETTER-1 (2017):** In progressive midgut NETs, ^177Lu-DOTATATE + octreotide improved PFS vs high-dose octreotide.
- **NETTER-2 (2024):** First-line PRRT + SSA in advanced Grade 2–3 NETs showed significant PFS benefit.

Eligibility:

- Strong uptake on ^68Ga-DOTATATE PET.
- Adequate renal and marrow function.

Administration:

- 4 cycles of ^177Lu-DOTATATE at 8-week intervals with amino acid infusion for renal protection.

Toxicities:

- Nausea (due to amino acid infusion), transient cytopenias, renal impairment (rare), late risk of myelodysplastic syndrome (MDS).

Exam Pearl: PRRT is **paradigm of theranostics** — same receptor used for diagnosis and treatment.

8.4 Targeted Therapy

A. Everolimus (mTOR inhibitor)

- **Mechanism:** Inhibits mammalian target of rapamycin (mTOR) pathway.
- **Dose:** 10 mg orally daily.
- **Trials:**
  - **RADIANT-3:** Improved PFS in pancreatic NETs (11 vs 4.6 months).
  - **RADIANT-4:** Improved PFS in non-functional gastrointestinal and lung NETs.
- **Toxicities:** Stomatitis, rash, hyperglycemia, non-infectious pneumonitis.

B. Sunitinib (tyrosine kinase inhibitor)

- **Mechanism:** Inhibits vascular endothelial growth factor receptor (VEGFR).
- **Trial:** Phase III study showed improved PFS (11.4 vs 5.5 months) in pancreatic NETs.
- **Toxicities:** Hypertension, fatigue, hand–foot syndrome, diarrhea.

C. Cabozantinib (multi-target TKI; CABINET trial, 2024)

- **Results:** Improved PFS in pancreatic and extrapancreatic NETs.
- **Emerging role** in patients progressing after SSAs/PRRT.

D. Other agents

- **Surufatinib (China trials SANET-p and SANET-ep):** demonstrated PFS benefit in both pancreatic and extra-pancreatic NETs.

Exam Pearl: Everolimus and sunitinib are standard targeted therapies in pancreatic NETs; cabozantinib is a new option post-SSA/PRRT

8.5 Chemotherapy

Indications:

- Pancreatic NETs with intermediate or high Ki-67 (often FDG PET-positive).
- Rapidly progressive or bulky disease not controlled by SSA or targeted therapy.

Regimens:

- **CAPTEM (Capecitabine + Temozolomide):**
  - High response rate (~30–40%) in pancreatic NETs.
  - Particularly effective in intermediate-grade, FDG-avid tumors.
  - Toxicities: cytopenias, fatigue, lymphopenia, rare myelodysplasia.
- **Streptozocin-based regimens:** Historically used; now less common.
- **FOLFOX (5-fluorouracil, leucovorin, oxaliplatin) or FOLFIRI (5-fluorouracil, leucovorin, irinotecan):** Used in higher-grade or refractory cases.

Exam Pearl: CAPTEM is the most effective chemotherapy for pancreatic NETs; rarely useful in small bowel NETs.

8.6 Liver-Directed Therapy

Rationale: Liver is the most common metastatic site; hepatic metastases often dominate prognosis.

Modalities:

- **Transarterial embolization (TAE):** Cuts off blood supply to liver metastases.
- **Transarterial chemoembolization (TACE):** Combines embolization with chemotherapy.
- **Transarterial radioembolization (TARE) with Yttrium-90 (Y-90):** Delivers intra-arterial radiation.
- **Ablation/resection:** Feasible in oligometastatic disease.

Precaution: Pre-procedure octreotide infusion to prevent carcinoid crisis.

Exam Pearl: Liver-directed therapy is palliative but can improve symptoms and prolong survival in selected patients with liver-dominant disease.

8.7 Treatment Sequencing (Simplified Algorithm)

1. **Grade 1–2, SSTR-positive:**
   - Start with SSA.
   - Progression → PRRT.
   - Further progression → targeted therapy (everolimus, sunitinib, cabozantinib).
   - Refractory/FDG-positive → chemotherapy (CAPTEM).
2. **Grade 3, well-differentiated NET:**
   - Dual-tracer imaging for biology.
   - DOTATATE+ → PRRT.
   - FDG+ → CAPTEM or FOLFOX.
   -

3. **Functional tumors:** Symptom control with SSA always first.

8.8 Teaching Pearls

- **SSA:** cornerstone, both for hormonal control and tumor stabilization.
- **PRRT (NETTER-1/2):** major advance; dual-tracer PET decides eligibility.
- **Everolimus and sunitinib:** established in pancreatic NETs.
- **Cabozantinib (CABINET trial, 2024):** new effective option.
- **CAPTEM:** best chemotherapy in pancreatic NETs.
- **Liver-directed therapy:** vital in liver-dominant disease.
- **Sequencing:** SSA → PRRT → targeted therapy → chemotherapy.

Section 9. Systemic Therapy for Poorly Differentiated Neuroendocrine Carcinomas (NECs)

9.1 Overview

- **Poorly differentiated neuroendocrine carcinomas (NECs)** include **small cell NEC (SCNEC)** and **large cell NEC (LCNEC)**, arising in gastrointestinal tract, pancreas, lung, and extra-pulmonary sites.
- They are **high-grade by definition**, with **Ki-67 usually >55%** and **molecular hallmarks of tumor protein p53 (TP53) mutation and retinoblastoma gene (RB1) loss**.
- NECs are **biologically similar to small cell lung carcinoma (SCLC)** and hence treated with **platinum-based chemotherapy** as the standard of care.

Prognosis:

- Median survival: 8–12 months in metastatic disease.
- Surgery ± adjuvant chemotherapy improves outcomes in localized disease, but relapse rates remain high.

9.2 First-Line Therapy

Platinum-Based Doublets

- **Cisplatin or carboplatin + etoposide (EP regimen):**
  - Standard of care, extrapolated from SCLC trials.
  - Response rates: 40–60%.
  - Median progression-free survival (PFS): 4–6 months.
  - Overall survival (OS): ~10–12 months.
- **Carboplatin + irinotecan (IP regimen):**
  - Alternative regimen; similar efficacy, sometimes better tolerated in GI NECs.

Clinical Choice:

- Cisplatin preferred in younger/fit patients.
- Carboplatin substituted in elderly or renal impairment.

9.3 Second-Line Therapy

Outcomes are poor after progression on platinum doublets. Options include:

- **FOLFIRI (5-fluorouracil, leucovorin, irinotecan):** modest activity.
- **FOLFOX (5-fluorouracil, leucovorin, oxaliplatin):** alternative regimen.
- **Temozolomide-based regimens (CAPTEM):** some activity in pancreatic NECs with intermediate Ki-67.
- **Amrubicin (Japan, not widely available):** modest benefit in relapsed NEC.

Median PFS in second-line: 2–3 months; OS rarely >6 months.

9.4 Immunotherapy

- **Single-agent PD-1/PD-L1 inhibitors** (pembrolizumab, nivolumab, atezolizumab) → low response rates (~5–10%) in NECs.
- **Dual checkpoint blockade (nivolumab + ipilimumab):** higher response (~20–25%), but durability limited.
- **MSI-high (microsatellite instability-high) or TMB-high (tumor mutational burden-high) NECs:** may benefit from immunotherapy, though rare.

Current role: Immunotherapy reserved for biomarker-selected patients or clinical trials.

9.5 Emerging Approaches

- **Chemo-immunotherapy (platinum + PD-L1 inhibitors):** standard in small cell lung carcinoma; under investigation in extrapulmonary NECs.
- **Targeted therapy:**
  - Limited role; NECs usually lack actionable mutations except rare BRAF V600E, KRAS, or ALK fusions.
- **PRRT (Peptide Receptor Radionuclide Therapy):**
  - Usually ineffective due to low SSTR expression.
  - May be considered in exceptional cases where DOTATATE PET uptake is strong.

9.6 Management of Localized NEC

- **Surgery:**
  - Recommended for localized gastrointestinal or pancreatic NEC if R0 resection possible.
- **Adjuvant chemotherapy:**
  - Platinum + etoposide given post-resection, extrapolated from SCLC.
- **Chemoradiation:**
  - Considered in locally advanced, unresectable but non-metastatic disease (e.g., rectal, esophageal NEC).

9.7 Prognosis

- **Localized disease (resected):** 3-year OS ~30–40% with adjuvant therapy.
- **Metastatic disease:** Median OS ~8–12 months.
- **Factors predicting worse prognosis:** liver metastases, Ki-67 >80%, poor performance status, TP53/RB1 loss, FDG-avid disease on PET.

9.8 Teaching Pearls

- NECs are **always high-grade**; do not confuse with NET Grade 3.
- **Morphology > Ki-67** in classification (NEC vs NET).
- **Platinum + etoposide** is standard first-line regimen.
- Relapse is almost universal; second-line therapies have low efficacy.
- **Immunotherapy** is not routine; use only in MSI-high/TMB-high or in trials.
- **Localized NEC:** multimodality therapy (surgery + adjuvant chemotherapy ± radiation).
- **Dual-tracer PET (DOTATATE + FDG):** NECs are almost always **FDG-positive, DOTATATE-negative**.

Section 10. Surgery and Locoregional Therapy in Neuroendocrine Neoplasms (NENs)

10.1 Role of Surgery in NENs

- Surgery remains the **only potentially curative treatment** for localized neuroendocrine tumors (NETs).
- Even in metastatic disease, surgery or cytoreduction can **improve survival and control hormone-related symptoms**.
- Decision-making requires **multidisciplinary tumor boards** (surgery, oncology, nuclear medicine, endocrinology).

Principles:

1. Aim for complete (R0) resection if feasible.
2. Regional lymphadenectomy is important (nodal metastases common even in small primaries).
3. Consider cytoreductive or debulking surgery if ≥70–90% of tumor burden can be removed.
4. Preservation of function and avoidance of unnecessary radicality is key.

10.2 Gastric Neuroendocrine Tumors

- **Type 1 and 2:**
  - Small, multifocal, indolent.
  - Managed by **endoscopic resection (endoscopic mucosal resection [EMR] or endoscopic submucosal dissection [ESD])** or surveillance.
  - Antrectomy may be considered in recurrent cases (removes source of hypergastrinemia).
- **Type 3 (sporadic):**
  - Solitary, often >2 cm, aggressive.
  - Managed with **radical gastrectomy + lymphadenectomy**.

10.3 Small Intestinal NETs

- **Standard:** Segmental resection with **mesenteric lymph node dissection**.
- **Intraoperative palpation:** essential due to **multifocality** (~20–25%).
- **Mesenteric fibrosis** may cause bowel ischemia → resection improves symptoms.
- **Debulking of liver metastases** considered if feasible.

10.4 Pancreatic NETs (pNETs)

Surgical Indications:

- All functional tumors (except insulinomas <2 cm).
- Non-functional tumors ≥2 cm.
- Smaller (<2 cm) non-functional tumors: observe in select patients (especially with Multiple Endocrine Neoplasia type 1, MEN1).

Types of Surgery:

- **Enucleation:** for small, superficial tumors away from the main pancreatic duct.
- **Pancreaticoduodenectomy (Whipple procedure):** for tumors in head/uncinate.
- **Distal pancreatectomy ± splenectomy:** for tumors in body/tail.
- **Central pancreatectomy:** rare, for mid-body lesions.

Cytoreductive Surgery:

- Considered in metastatic disease if >70% burden removable.
- Symptom control (hormone secretion) is a major indication.

10.5 Appendiceal NETs

- **<1 cm:** Simple appendectomy sufficient.
- **1–2 cm:** Appendectomy adequate if no risk factors; right hemicolectomy if base involvement, mesoappendiceal invasion >3 mm, or lymphovascular invasion.
- **>2 cm:** Right hemicolectomy with lymphadenectomy.
- Prognosis excellent overall.

10.6 Colorectal NETs

- **Rectal NETs:**
  - ≤1 cm, Grade 1 → Endoscopic resection curative.
  - 1–2 cm → Endoscopic or local excision if low grade; radical resection if high grade or lymphovascular invasion.
    - 2 cm → Radical surgery with nodes.
- **Colonic NETs:**
  - Rare, aggressive.
  - Managed with oncologic colectomy (segmental resection + lymphadenectomy).

10.7 Pulmonary NETs

- **Typical Carcinoid (TC) and Atypical Carcinoid (AC):**
  - Surgical resection (lobectomy or sleeve resection) with **systematic mediastinal lymph node dissection**.
  - Wedge resections discouraged unless high-risk patients.
- **Large Cell NEC (LCNEC) and Small Cell NEC (SCNEC):**
  - Managed as small cell lung cancer — chemotherapy ± radiation.
  - Surgery rarely indicated except in early stage LCNEC.

10.8 Locoregional Therapy for Liver Metastases

The **liver is the most common site of metastasis**. Locoregional options are crucial when systemic disease is liver-dominant.

A. Surgical Resection

- Preferred in resectable disease with preserved liver function.
- 5-year survival up to 60–70% in selected cases.
- Recurrence is common, but re-resection feasible.

B. Cytoreductive Surgery + Ablation

- Combine resection of dominant lesions with **radiofrequency ablation (RFA)** or microwave ablation for smaller deposits.

C. Transarterial Therapies

- **Transarterial embolization (TAE):** occludes blood supply.
- **Transarterial chemoembolization (TACE):** embolization + chemotherapy.
- **Transarterial radioembolization (TARE, Yttrium-90 microspheres):** radiation delivered intra-arterially.

D. Ablative Techniques

- Radiofrequency ablation (RFA) and microwave ablation: useful for <3 cm lesions.

E. Liver Transplantation

- Rarely considered in highly selected patients (young, liver-only disease, Ki-67 <10%, stable disease, SSTR-positive).

10.9 Perioperative Considerations

- **Carcinoid crisis:**
  - Triggered by anesthesia or surgery.
  - Severe flushing, hypotension, bronchospasm.
  - Prevention: continuous **octreotide infusion (50–100 mcg/hour)** perioperatively.
- **Multifocality check:** Mandatory in small bowel NETs.
- **MEN1-associated pNETs:** high recurrence risk; surgical extent tailored.

10.10 Teaching Pearls (Exam-Oriented)

- Surgery is **curative only in localized disease**, but also improves survival in selected metastatic NETs.
- **Small bowel NETs:** Always palpate entire bowel → multifocal.
- **pNETs:** Functional tumors → always operate.
- **Appendix NETs:** Size + location dictate appendectomy vs hemicolectomy.
- **Rectal NETs:** ≤1 cm → endoscopic; >2 cm → radical surgery.
- **Liver metastases:** Resection + ablation if possible; otherwise TAE/TACE/TARE.
- **Carcinoid crisis prophylaxis:** Octreotide infusion mandatory.
- **Cytoreduction threshold:** ≥70–90% resection beneficial for survival/symptom control.

Section 11. Role of Radiotherapy in Neuroendocrine Neoplasms (NENs)

11.1 Introduction

Historically, radiotherapy (RT) was considered of **limited utility** in neuroendocrine tumors (NETs) due to their **slow-growing, radioresistant biology**. However, in the era of **precision RT techniques** (stereotactic radiotherapy, radiosurgery, proton therapy) and **theranostic radiolig and therapies** (PRRT), the role of radiation in NENs has significantly expanded.

Key roles include:

1. **Definitive RT** for unresectable or locally advanced tumors (rare).
2. **Adjuvant/combined RT** in poorly differentiated neuroendocrine carcinomas (NECs).
3. **Palliative RT** for symptom control (pain, obstruction, bleeding, neurological symptoms).
4. **Stereotactic radiotherapy (SRT)/Stereotactic radiosurgery (SRS):** for oligometastatic or oligoprogressive disease (especially brain, bone, liver).
5. **Peptide Receptor Radionuclide Therapy (PRRT):** systemic targeted radionuclide therapy — a unique radiotherapeutic approach in NETs.

11.2 Radiobiological Considerations

- **Well-differentiated NETs (Grade 1–2):**
  - Slow doubling time, low proliferation fraction.
  - Less responsive to conventional fractionated RT.
- **Poorly differentiated NECs:**
  - Aggressive, high Ki-67, rapid proliferation.
  - Radiosensitive, similar to small cell lung carcinoma (SCLC).
- **Clinical implication:**
  - **NECs** → RT effective in local control or combined chemoradiation.
  - **NETs** → RT useful for palliation or stereotactic settings.

11.3 Conventional External Beam Radiotherapy (EBRT)

A. Gastrointestinal and Pancreatic NETs

- Limited role in primary control.
- May be used for:
  - **Unresectable locally advanced disease** (rare).
  - **Symptom palliation** (pain, obstruction, bleeding).

B. Poorly Differentiated NECs

- Managed similar to SCLC or extrapulmonary small cell carcinomas.
- **Sites:**
  - *Esophagus/Rectum/Anal canal:* Definitive chemoradiation is an option.
  - *Pancreas/Colon:* Adjuvant chemoradiation in select cases.
- **Regimens:**
  - Cisplatin/Carboplatin + Etoposide with 50–60 Gy RT.

11.4 Stereotactic Radiosurgery (SRS) and Stereotactic Body Radiotherapy (SBRT/SRT)

- **Indications:**
  - Oligometastatic disease.
  - Oligoprogression on systemic therapy.
  - Symptom control in brain, bone, liver, or lung metastases.
- **Advantages:**
  - High-dose per fraction → effective even in ―radioresistant‖ histologies.
  - Short treatment course.
- **Clinical data:**
  - **Brain metastases:** SRS effective in NECs, local control >80%.
  - **Liver metastases:** SBRT achieves local control ~70–90% at years.
  - **Bone metastases:** Rapid pain relief; especially useful in spinal cord compression.

11.5 Palliative Radiotherapy

- **Indications:**
  - Painful bone metastases.
  - Symptomatic brain metastases.
  - Spinal cord compression.
  - Bleeding tumors (rectal NETs, gastric NETs).
- **Typical regimens:**
  - 8 Gy single fraction (bone pain).
  - 20 Gy/5 fractions or 30 Gy/10 fractions (brain, soft tissue).
  - 30–40 Gy in 10–15 fractions (hemorrhage control).

Exam Pearl: Even though NETs are indolent, palliation from RT can be **rapid and effective**.

11.6 Peptide Receptor Radionuclide Therapy (PRRT)

Although technically a **nuclear medicine therapy**, PRRT represents a **form of systemic radiotherapy**:

- **Agent:** Lutetium-177 (^177Lu)-DOTATATE (beta-emitter).
- **Mechanism:** Delivers targeted internal radiation to somatostatin receptor-expressing NETs.
- **Indications:** Advanced, progressive, SSTR-positive NETs.
- **Evidence:** NETTER-1 and NETTER-2 trials — significant improvement in PFS, response rates.
- **Toxicities:** Nausea, marrow suppression, rare renal dysfunction, long-term risk of myelodysplastic syndrome.

11.7 Proton Therapy and Advanced RT

- **Proton beam therapy:** Rarely used, but may be considered in pediatric NENs or re-irradiation settings to spare normal tissue.
- **Carbon ion therapy:** Under investigation; may offer higher biological effectiveness in resistant tumors.

11.8 Practical Decision-Making

- **Well-differentiated NETs:**
  - Surgery/systemic therapy preferred.
  - RT used mainly for palliation or oligometastatic control.
- **Poorly differentiated NECs:**
  - RT has a **definitive role** in combined chemoradiation or as palliative therapy.
- **Metastatic disease:**
  - RT plays supportive role — local control, symptom relief, selected oligometastatic ablation.

11.9 Teaching Pearls (Exam-Oriented)

- **NETs:** relatively radioresistant → RT mainly for palliation/SBRT.
- **NECs:** radiosensitive → RT + chemotherapy standard in localized disease.
- **SRS/SBRT:** excellent for oligometastatic brain, liver, bone disease.
- **PRRT:** systemic targeted radiotherapy, now a **cornerstone therapy** in NETs.
- **Carcinoid crisis prophylaxis:** Peri-RT octreotide infusion if bulky, functional NET.
- **RT dose:** use hypofractionated/SBRT regimens in NETs for efficacy.

Section 12. Special Considerations in Neuroendocrine Neoplasms (NENs)

12.1 Hereditary Syndromes

About **5–10% of NENs** occur in the context of hereditary cancer syndromes. Recognition is crucial for **screening, counseling, and surgical planning**.

A. Multiple Endocrine Neoplasia type 1 (MEN1)

- **Gene:** MEN1 (menintumor suppressor).
- **Tumor spectrum:**
  - Parathyroid adenomas (90%).
  - Pituitary adenomas (40%).
  - Pancreatic neuroendocrine tumors (pNETs) (30–70%).
- **pNETs in MEN1:**
  - Often multiple, non-functional.
  - Functional subtypes: gastrinoma, insulinoma.
  - Higher recurrence after surgery.
- **Screening:** annual biochemical + MRI/EUS (endoscopic ultrasound) of pancreas from age 10–12 yrs.

B. Von Hippel–Lindau (VHL) Syndrome

- **Gene:** VHL (chromosome 3p25).
- **Tumor spectrum:** renal cell carcinoma, pheochromocytoma, hemangioblastomas, pancreatic cysts.
- **Pancreatic NETs:** often multiple, non-functional, indolent.
- **Surveillance:** MRI abdomen every 1–2 yrs.

C. Neurofibromatosis type 1 (NF1, von Recklinghausen's disease)

- **Gene:** NF1, encodes neurofibromin (tumor suppressor).
- **Associated NETs:** duodenal somatostatinomas (often peri-ampullary).
- **Clinical features:** café-au-lait spots, neurofibromas, optic gliomas.

D. Tuberous Sclerosis Complex (TSC)

- **Genes:** TSC1 (hamartin), TSC2 (tuberin).
- **Associated with:** cortical tubers, renal angiomyolipomas, subependymal giant cell astrocytomas.
- **Rare association:** pancreatic NETs, often indolent.

E. RET Proto-Oncogene Mutations (MEN2 Syndromes)

- **Tumor spectrum:** medullary thyroid carcinoma, pheochromocytoma, parathyroid hyperplasia.
- **NET association:** primarily medullary thyroid carcinoma (MTC), which is a calcitonin-secreting neuroendocrine carcinoma of the thyroid.

F. Succinate Dehydrogenase (SDHx) Mutations

- **Spectrum:** paragangliomas, pheochromocytomas, gastrointestinal stromal tumors.
- **Occasional overlap with NETs.**

Clinical Relevance:

- Family history, young age, multiple primaries → suspect hereditary syndrome.
- Genetic counseling and germline testing essential.

Exam Pearl: MEN1 → multiple pNETs; NF1 → peri-ampullary somatostatinoma; VHL → indolent pNETs.

12.2 Carcinoid Heart Disease (CHD)

Pathophysiology:

- Serotonin and vasoactive substances secreted by midgut NETs bypass liver metabolism (due to liver metastases) → fibrosis of right-sided heart valves.
- Leads to **tricuspid regurgitation** and **pulmonary stenosis**.

Clinical Features:

- Right heart failure (edema, ascites, fatigue).
- Cardiac murmur.

Diagnosis:

- **Echocardiography:** thickened, immobile tricuspid/pulmonary valves.
- **NT-proBNP (N-terminal pro–brain natriuretic peptide):** biomarker of cardiac strain.

Management:

- Control serotonin with **somatostatin analogues (SSA)**.
- Valve replacement surgery in severe cases.
- Pre-procedure octreotide infusion to prevent crisis.

Exam Pearl: Carcinoid heart disease affects right heart because serotonin is inactivated in pulmonary circulation; left heart involvement only if bronchial carcinoid or intracardiac shunt.

12.3 Pregnancy and NENs

- NETs are rare in pregnancy.
- Challenges:
  - Hormonal syndromes may mimic pregnancy-related symptoms.
  - Imaging limited (avoid radiation; MRI without gadolinium preferred).
- Management:
  - Surgery for localized, resectable disease if safe.
  - SSA (octreotide, lanreotide) considered safe in pregnancy if needed for hormone control.
  - PRRT, targeted therapies, and chemotherapy contraindicated.
- Multidisciplinary decision-making essential.

Exam Pearl: SSAs can be cautiously used in pregnancy; PRRT contraindicated.

12.4 Pediatric Neuroendocrine Tumors

- **Rare (<1% of pediatric tumors).**
- Common sites: appendix (most frequent), pancreas (functional tumors).
- **Appendiceal NETs:** often incidental, prognosis excellent.
- **pNETs in children:** often associated with MEN1, VHL, or NF1.
- **Management:**
  - Appendiceal NETs follow adult algorithms (appendectomy vs hemicolectomy).
  - pNETs: surgery for functional or >2 cm lesions; surveillance for small, indolent tumors.
- Outcomes generally favorable except in NECs, which behave aggressively.

Exam Pearl: Pediatric appendiceal NETs have an excellent prognosis; genetic syndromes must always be considered.

12.5 Other Considerations

Mixed Neuroendocrine–Non-Neuroendocrine Neoplasms (MiNENs)

- Defined as tumors with ≥30% neuroendocrine and ≥30% non-neuroendocrine component (usually adenocarcinoma).
- Management guided by **more aggressive component** (often NEC-like).

Secondary Malignancies

- Long survival in NET patients → higher risk of synchronous/metachronous second cancers (breast, colon, prostate).
- Lifelong surveillance needed.

Quality of Life & Survivorship

- Functional syndromes (flushing, diarrhea, hypoglycemia).
- Late effects of therapies (PRRT marrow suppression, gallstones after SSA).
- Multidisciplinary survivorship care important.

12.6 Teaching Pearls (Exam-Oriented)

- **MEN1:** multiple pNETs, high recurrence after surgery.
- **NF1:** peri-ampullary somatostatinomas.
- **VHL:** indolent, often multiple pNETs.
- **Carcinoid heart disease:** right-sided valves, NT-proBNP useful, echo diagnostic.
- **Pregnancy:** SSA safe; avoid PRRT, chemo, targeted agents.
- **Pediatric NETs:** appendiceal NETs most common, excellent prognosis.
- **MiNENs:** ≥30% each component; treat as NEC if high-grade.

Section 13. Follow-Up and Survivorship in Neuroendocrine Neoplasms (NENs)

13.1 Importance of Follow-Up

- NETs are **chronic diseases** with long natural history.
- Recurrence may occur even **10–15 years after initial diagnosis**, especially in well-differentiated tumors.
- Surveillance is essential for:
    - Early detection of recurrence or progression.
    - Monitoring functional syndromes (carcinoid, gastrinoma, insulinoma, etc.).
    - Managing treatment-related late effects.
    - Screening for second malignancies.

13.2 Principles of Surveillance

1. **Tailored by grade and stage**: Low-grade NETs require longer surveillance; NECs have shorter intervals due to rapid progression.
2. **Multimodal approach**: Clinical, biochemical, imaging.
3. **Individualized**: Consider genetic syndromes (MEN1, VHL, NF1, TSC) where lifelong monitoring is required.

13.3 Clinical Follow-Up

- **History:** Symptoms of hormone secretion (flushing, diarrhea, hypoglycemia, peptic ulcers, rash).
- **Physical examination:** Abdominal masses, hepatomegaly, signs of carcinoid heart disease (murmur, edema).
- **Functional assessment:** Quality of life, symptom diaries for hormone-producing NETs.
- **Cardiac evaluation:** For patients with carcinoid syndrome → baseline and periodic echocardiography + NT-proBNP (N-terminal pro–brain natriuretic peptide).

13.4 Biochemical Follow-Up

- **Chromogranin A (CgA):**
  - Useful in most NETs, especially for trend monitoring.
  - Limitations: false positives with proton pump inhibitors (PPIs), atrophic gastritis, renal failure.
- **Pancreastatin:** more specific, less influenced by PPIs.
- **Hormone-specific markers:**
  - *Carcinoid syndrome:* 24-hour urinary 5-HIAA (5-hydroxyindoleacetic acid).
  - *Insulinoma:* fasting insulin, C-peptide.
  - *Gastrinoma:* fasting gastrin ± secretin stimulation test.
  - *VIPoma:* serum vasoactive intestinal peptide (VIP).
  - *Glucagonoma:* serum glucagon.
  - *Somatostatinoma:* serum somatostatin.

Exam Pearl: Always stop PPIs at least 2 weeks before testing chromogranin A.

13.5 Imaging Surveillance

- **Cross-sectional imaging:**
  - Contrast-enhanced triphasic CT or MRI every 6–12 months.
  - MRI preferred for liver-dominant disease (greater sensitivity).
- **Functional imaging:**
  - ^68Ga-DOTATATE PET/CT (somatostatin receptor imaging): baseline staging and repeated at progression.
  - ^18F-FDG PET/CT (fluorodeoxyglucose): for NECs and NET Grade 3.
- **Endoscopic surveillance:**
  - Rectal NETs after local excision (colonoscopy).
  - Gastric NETs Type 1 and 2 (gastroscopy every 1–2 years).

- **Echocardiography:**
  - Every 1–2 years in patients with carcinoid syndrome, more frequent if symptomatic.

13.6 Suggested Follow-Up Schedules (NCCN/ENETS Recommendations)

Well-differentiated NETs (Grade 1–2):

- Clinical + labs + imaging every 6–12 months for first 5 years.
- Annually thereafter, lifelong due to late recurrences.

Well-differentiated NET Grade 3:

- Every 3–6 months initially, given higher relapse risk.

Poorly differentiated NECs:

- Every 2–3 months for first 2 years.
- Thereafter 6 monthly if patient remains in remission (rare).

Post-curative resection of appendiceal NET <1 cm:

- Usually no routine follow-up needed (if no adverse features).

13.7 Survivorship Issues

A. Late Recurrence

- NETs can recur decades later.
- Patients should be counseled about **lifelong vigilance**.

B. Functional Syndromes

- Hormone hypersecretion may persist or recur despite tumor control.
- Requires chronic SSA therapy, supportive medications (antidiarrheals, PPIs, glucose control).

C. Carcinoid Heart Disease

- Progressive; may require valve replacement.
- Routine cardiac follow-up essential.

D. Treatment-Related Toxicities

- **Somatostatin analogues:** gallstones, steatorrhea, glucose intolerance.
- **PRRT (Peptide Receptor Radionuclide Therapy):** myelosuppression, nephrotoxicity, risk of myelodysplastic syndrome.
- **Everolimus:** metabolic syndrome, pneumonitis.
- **Sunitinib/cabozantinib:** hypertension, hand–foot syndrome, proteinuria.

E. Psychological and Social Issues

- Chronic disease course → anxiety, depression, ―living with cancer‖ burden.
- Genetic syndromes → family screening and counseling required.
- Survivorship programs must address nutrition, fertility, and long-term psychosocial care.

13.8 Second Malignancies

- NET patients have **higher risk of synchronous or metachronous cancers** (colon, breast, prostate, kidney).
- Routine age-appropriate cancer screening (mammogram, colonoscopy, PSA, Pap smear) should be maintained.

13.9 Teaching Pearls (Exam-Oriented)

- NETs can recur even after 10 years → **lifelong surveillance**.
- CgA useful but nonspecific; pancreastatin is more specific.
- Functional imaging (^68Ga-DOTATATE PET) superior to Octreoscan.
- Carcinoid syndrome → NT-proBNP + echocardiography for cardiac monitoring.

- Follow-up intervals:
  - NET G1/2: 6–12 months.
  - NET G3: 3–6 months.
  - NEC: 2–3 months early.
- Survivorship includes monitoring late toxicity (PRRT marrow, SSA gallstones).

Section 14. Emerging Perspectives and Future Directions in Neuroendocrine Neoplasms (NENs)

14.1 Introduction

The last two decades have seen a **paradigm shift** in the management of neuroendocrine tumors (NETs) and neuroendocrine carcinomas (NECs). Advances in **molecular biology, imaging, radionuclide therapy, and targeted agents** have transformed outcomes. Ongoing research aims to further personalize care, improve survival, and enhance quality of life.

14.2 Novel Systemic Therapies

A. Radioligand Therapies Beyond ^177Lu-DOTATATE

- **Actinium-225 (^225Ac)-DOTATATE:** Alpha-emitter with higher linear energy transfer; effective in PRRT-refractory NETs.
- **Terbium-161 (^161Tb):** Beta emitter with higher Auger electron yield; under clinical evaluation.
- **Combination PRRT + chemotherapy (PRCRT, peptide receptor chemo-radionuclide therapy):** synergistic activity shown in pilot studies.

B. Combination Therapies

- **PRRT + Immune Checkpoint Inhibitors:** being studied to enhance immune-mediated killing after radiation-induced antigen release.
- **PRRT + Everolimus or Sunitinib:** trials ongoing to improve durability of responses.
- **Chemo-immunotherapy in NECs:** platinum–etoposide + PD-L1 inhibitors (like small cell lung carcinoma).

C. New Targeted Therapies

- **Cabozantinib (CABINET trial, 2024):** showed progression-free survival (PFS) benefit in NETs post-SSA/PRRT.
- **Surufatinib (China, SANET trials):** VEGFR/FGFR/CSF1R inhibitor, approved in China.
- **Bevacizumab (anti-VEGF antibody):** in trials with SSAs and chemotherapy.

14.3 Immunotherapy

- **Checkpoint inhibitors:** generally low activity in well-differentiated NETs.
- **Dual blockade (nivolumab + ipilimumab):** modest activity in high-grade NECs.
- **MSI-high (microsatellite instability-high) / TMB-high (tumor mutational burden-high) NENs:** rare but responsive to PD-1 inhibitors.
- **Future:** Biomarker-driven immunotherapy combinations under active evaluation.

14.4 Advances in Imaging

- **Dual-tracer PET (DOTATATE + FDG):**
  - Now standard for grading and prognosis.
  - Guides sequencing of therapies (PRRT vs chemotherapy).
- **Artificial Intelligence (AI) / Radiomics:**
  - Predicts Ki-67 index, SSTR expression, and progression risk.
  - Automated tumor burden quantification in PET/CT scans.
- **Novel tracers:**
  - Fibroblast activation protein inhibitors (FAPI-PET) for SSTR-negative NETs.
  - CXCR4-targeted tracers in aggressive NET/NEC.

14.5 Genomic and Molecular Advances

- **Molecular profiling:** distinguishes NET G3 (MEN1, ATRX, DAXX) from NEC (TP53, RB1, MYC).
- **Circulating tumor DNA (ctDNA):** liquid biopsy for monitoring disease burden, emerging as non-invasive surveillance tool.
- **Multi-omics:** integrating genomics, transcriptomics, and metabolomics to stratify patients.

14.6 Personalized and Precision Medicine

- **Theranostics paradigm:** NETs are prototypes of precision oncology — diagnosis and therapy based on same molecular target (SSTR2).
- **Patient stratification:**
  - DOTATATE-positive → PRRT.
  - FDG-positive → chemotherapy.
  - Dual-positive → sequential or combination approaches.
- **AI-driven therapy selection:** predictive models incorporating imaging + genomics under development.

14.7 Role of Radiotherapy Innovations

- **Stereotactic body radiotherapy (SBRT):** expanding role in oligometastatic NETs (liver, bone, brain).
- **Particle therapy:** Proton and carbon ion therapy trials ongoing, may benefit resistant NECs.
- **Integration with PRRT:** sequential or concurrent RT + PRRT approaches under study.

14.8 Survivorship and Supportive Care

- **Focus shifting from survival to survivorship:**
  - Long-term management of functional syndromes.
  - Monitoring and treating late effects of SSA, PRRT, and targeted agents.
  - Cardiac surveillance in carcinoid heart disease.
- **Psychosocial support:** NETs are chronic, anxiety-provoking; support groups (e.g., NET Patient Foundation) increasingly important.
- **Digital health & tele-oncology:** remote monitoring of symptoms and biomarkers.

14.9 Future Research Directions

1. **Improving PRRT efficacy:** novel radionuclides, combination regimens, retreatment strategies.
2. **Expanding immunotherapy:** biomarker-driven trials, combinations with radiation and targeted therapy.
3. **Refining prognostic models:** incorporation of dual-tracer PET and molecular signatures.
4. **Early detection in hereditary syndromes:** MEN1, VHL, NF1, TSC surveillance programs.
5. **Pediatric NENs:** global registries and tailored treatment algorithms.
6. **Liquid biopsy and AI tools:** early detection of relapse, prediction of therapy response.

14.10 Teaching Pearls (Exam-Oriented)

- **NETs are the prototype of theranostics**: DOTATATE PET → PRRT.
- **Next-gen PRRT:** alpha emitters (^225Ac-DOTATATE) under trials.
- **Cabozantinib (CABINET, 2024):** new targeted therapy option.
- **Dual-tracer imaging:** DOTATATE + FDG is now standard for biology-based decision-making.
- **Molecular profiling separates NET G3 from NEC** (ATRX/DAXX/MEN1 vs TP53/RB1).
- **Survivorship issues are critical**: carcinoid heart disease, PRRT toxicity, SSA gallstones.
- **AI & liquid biopsy** → emerging precision tools in NEN care.

***

TEST YOUR UNDERSTANDING

Q1.

Which of the following is **most specific** for neuroendocrine differentiation in immunohistochemistry?
A. Synaptophysin
B. Chromogranin A
C. CD56
D. INSM1

Q2.

A 45-year-old woman with **MEN1** has multiple pancreatic lesions. Which biochemical marker is **most useful** to screen for Zollinger–Ellison syndrome?
A. Serum insulin
B. Serum gastrin
C. Serum glucagon
D. Serum VIP

Q3.

Which of the following features **distinguishes NET Grade 3 from NEC**?
A. Ki-67 index >20%
B. Necrosis
C. TP53/RB1 status
D. Mitotic count >20/2 mm²

Q4.

In the **NETTER-1 trial**, Lutetium-177 DOTATATE was compared against:
A. High-dose lanreotide
B. High-dose octreotide LAR
C. Everolimus
D. Sunitinib

Q5.

The **most common site** of small intestinal NETs is:
A. Duodenum
B. Jejunum
C. Ileum
D. Cecum

Q6.

Which **appendiceal NET feature** warrants right hemicolectomy?
A. Tumor size 0.7 cm, tip location
B. Tumor size 1.2 cm, base involvement
C. Tumor size 0.9 cm, confined to submucosa
D. Tumor size 0.8 cm, no LVI

Q7.

Which syndrome is **not typically associated** with neuroendocrine tumors?
A. MEN1
B. VHL
C. Li-Fraumeni
D. NF1

Q8.

In carcinoid heart disease, which valve is **most commonly affected**?
A. Aortic
B. Mitral
C. Tricuspid
D. Pulmonic

Q9.

^68Ga-DOTATATE PET/CT uptake correlates best with:
A. Ki-67 index
B. Somatostatin receptor 2A expression
C. p53 mutation
D. RB1 loss

Q10.

Which of the following drugs has **demonstrated antiproliferative benefit** in NETs in the PROMID trial?
A. Lanreotide
B. Octreotide LAR
C. Everolimus
D. Sunitinib

Q11.

Which is the **preferred chemotherapy regimen** in metastatic NECs?
A. CAPTEM (Capecitabine + Temozolomide)
B. Platinum + Etoposide
C. FOLFOX
D. Streptozocin + 5FU

Q12.

Which gastric NET subtype is **most aggressive**?
A. Type 1 (autoimmune gastritis)
B. Type 2 (MEN1/Zollinger–Ellison)
C. Type 3 (sporadic)
D. Type 4 (rare variant)

Q13.

Which genetic alteration is **most frequent in pancreatic NETs**?
A. TP53 mutation
B. RB1 loss
C. MEN1 mutation
D. MYC amplification

Q14.

Which biochemical test confirms **carcinoid syndrome**?
A. Serum CgA
B. 24-hour urinary 5-HIAA
C. Serum insulin
D. Serum glucagon

Q15.

Which liver-directed therapy uses **radioactive microspheres**?
A. TAE
B. TACE
C. RFA
D. TARE

Q16.

The **Ki-67 cutoff for Grade 2 NET** according to WHO 2022 is:
A. ≤2%
B. 3–20%
C. >20%
D. >55%

Q17.

Which lung NET subtype has the **best prognosis**?
A. Typical carcinoid
B. Atypical carcinoid
C. Large cell NEC
D. Small cell NEC

Q18.

Which of the following is **not a functional pancreatic NET**?
A. Insulinoma
B. Gastrinoma
C. Glucagonoma
D. Adenocarcinoma

Q19.

Carcinoid crisis during surgery is prevented by:
A. Preoperative steroids
B. Octreotide infusion
C. Beta-blockers
D. Cisplatin premedication

Q20.

Which marker helps **differentiate NET from NEC**?
A. Ki-67
B. p53/Rb immunohistochemistry
C. Synaptophysin
D. Chromogranin

Q21.

Median survival in metastatic NEC treated with platinum chemotherapy is approximately:
A. 1–2 years
B. 8–12 months
C. 3–5 years
D. >7 years

Q22.

Which targeted therapy showed PFS benefit in **RADIANT-3 trial**?
A. Everolimus
B. Sunitinib
C. Cabozantinib
D. Bevacizumab

Q23.

In NETTER-2 (2024), the major finding was:
A. PRRT effective in first-line Grade 2–3 NETs
B. Everolimus improves OS
C. Sunitinib active in midgut NETs
D. Cabozantinib is superior to SSA

Q24.

Which functional NET syndrome is characterized by **watery diarrhea, hypokalemia, achlorhydria (WDHA)**?
A. Glucagonoma
B. Gastrinoma
C. VIPoma
D. Insulinoma

Q25.

Which of the following is the **prototype of theranostics in oncology**?
A. HER2 breast cancer
B. NET with DOTATATE PET + PRRT
C. EGFR-mutant NSCLC
D. BRAF melanoma

Answers and Explanations

Q1. B. Chromogranin A

- Chromogranin A is more **specific** for neuroendocrine differentiation, while synaptophysin is more sensitive but less specific. INSM1 is sensitive/specific but not yet universally used.

Q2. B. Serum gastrin

- Zollinger–Ellison syndrome = gastrinoma → markedly elevated fasting serum gastrin with low gastric pH confirms diagnosis.

Q3. C. TP53/RB1 status

- Both NET G3 and NEC have high Ki-67/mitoses. Morphology and molecular surrogates (TP53 mutation, RB1 loss) distinguish NEC.

Q4. B. High-dose octreotide LAR

- NETTER-1 compared ^177Lu-DOTATATE vs high-dose octreotide LAR in progressive midgut NETs, showing dramatic PFS benefit.

Q5. C. Ileum

- The ileum is the commonest site of small intestinal NETs, often presenting with mesenteric fibrosis and carcinoid syndrome.

Q6. B. Tumor size 1.2 cm, base involvement

- Right hemicolectomy indicated for >2 cm or 1–2 cm with risk factors (base, LVI, mesoappendix invasion >3 mm).

Q7. C. Li-Fraumeni

- Associated with sarcomas, breast, adrenal cortical carcinoma; not NENs. MEN1, VHL, NF1 predispose to NETs.

Q8. C. Tricuspid

- Carcinoid heart disease classically involves **right-sided valves**: tricuspid regurgitation and pulmonary stenosis.

Q9. B. Somatostatin receptor 2A expression

- DOTATATE uptake directly reflects somatostatin receptor subtype 2A density, guiding PRRT eligibility.

Q10. B. Octreotide LAR

- PROMID (2009): Octreotide LAR improved progression-free survival in midgut NETs.

Q11. B. Platinum + Etoposide

- NECs are biologically like small cell carcinoma; standard regimen is platinum + etoposide.

Q12. C. Type 3 (sporadic)

- Gastric NET type 3: solitary, >2 cm, aggressive, requires gastrectomy. Types 1 & 2 are indolent.

Q13. C. MEN1 mutation

- MEN1, ATRX, and DAXX mutations are common in pancreatic NETs; TP53/RB1 in NECs.

Q14. B. 24-hour urinary 5-HIAA

- Gold standard for carcinoid syndrome diagnosis; correlates with serotonin secretion.

Q15. D. TARE

- Transarterial radioembolization (TARE) uses radioactive microspheres (Yttrium-90).

Q16. B. 3–20%

- WHO 2022 grading: Grade 1 ≤2%, Grade 2 = 3–20%, Grade 3 >20%.

Q17. A. Typical carcinoid

- Typical carcinoids have <2 mitoses/2 mm², no necrosis, 5-year survival >90%.

Q18. D. Adenocarcinoma

- Adenocarcinoma is not a functional NET; insulinoma, gastrinoma, glucagonoma are functional.

Q19. B. Octreotide infusion

- Continuous perioperative octreotide infusion prevents carcinoid crisis during anesthesia/surgery.

Q20. B. p53/Rb immunohistochemistry

- Helps separate NET G3 (wild-type) from NEC (abnormal p53, Rb loss).

Q21. B. 8–12 months

- Metastatic NEC median OS with platinum chemo ~8–12 months.

Q22. A. Everolimus

- RADIANT-3: Everolimus prolonged PFS in pancreatic NETs.

Q23. A. PRRT effective in first-line Grade 2–3 NETs

- NETTER-2 showed benefit of ^177Lu-DOTATATE earlier in the disease course.

Q24. C. VIPoma

- VIPoma → watery diarrhea, hypokalemia, achlorhydria (WDHA syndrome).

Q25. B. NET with DOTATATE PET + PRRT

- Neuroendocrine tumors are the **prototype of theranostics**, using same target for diagnosis and therapy.

AROI - ICRO ACADEMIC CALENDAR 2026

ASSOCIATION OF RADIATION ONCOLOGISTS OF INDIA
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AROI – YROC 2026

Venue	Dates	Coordinator	Contact No.	Theme
NIMHANS Convention Centre, Bengaluru, Karnataka	24-25 Jan 2026	Dr S D ShamSundar	7760612035	Igniting the Future of Radiation Oncology: Inspire, Innovate, Impact.

ICRO – SUN PG

Venue	Dates	Coordinator	Contact No.	Theme
JN Medical College, AMU, Aligarh	Apr 2026	Dr Md. Shadab Alam	9634464879	TBD
Cancer Institute, Adyar, Chennai	July 2026	Dr Priya Iyer	9498082772	TBD
Cancer Hospital, IGMC, Shimla	Sep 2026	Dr Manish Gupta	9418455673	TBD

ICRO - INTAS RADIOBIOLOGY COURSE (Prof. Manoj Gupta)

Venue	Dates	Coordinator	Contact No.	Theme
SGRR Institute of Medical & Health Sciences, Dehradun	Nov 2026	Dr Manoj Gupta	9418470607	RADIOBIOLOGY

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AROI – ESTRO Teaching Courses

Course	Dates	Coordinator	Contact No.	Venue
12th AROI-ESTRO Advanced Technologies	29 Jan – 1 Feb 2026	Dr Rakesh Kapoor	9872648344	PGIMER, Chandigarh
9th AROI-ESTRO Gynaec	26–29 Mar 2026	Dr Tapas Kumar Dora	9464448823	HBCH & RC, New Chandigarh
4th AROI-ESTRO Head & Neck	4–6 June 2026	Dr Shalini Singh	9335904587	SGPGIMS, Lucknow

Best of ASTRO (BOA)

Dates	Coordinator	Contact No.	Venue
May 2026	Dr Kanika Sood Sharma (Tentative)	9899320923	Narayana Health, New Delhi

46th AROICON 2026

Venue	Dates	Coordinator	Contact No.	Host Institution
Hyderabad Convention Centre	03–06 Dec 2026	Dr Vijay Karan Reddy	9912320002	Apollo Cancer Institute, Hyderabad