Radionuclide therapy by means of selective intraarterial radiotherapy (SIRT) and intravascular irradiation with open radionuclides

Recommendation by the German Commission on Radiological Protection

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Radionuklidtherapie mittels selektiver intraarterieller Radiotherapie (SIRT) und intravasale Bestrahlung mit offenen Radionukliden

Empfehlung der Strahlenschutzkommission

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1 Introduction and definition of topic

Radiotherapy with open radionuclides – in general beta emitters – has been established in medicine more than fifty years ago. Ideally, radioactive substances (radiopharmaceuticals) concentrate specifically in the seat of the disease after intravenous injection. Apart from knowledge of radiobiology and radiological protection, a therapy of this kind demands a profound understanding of physiological and pathophysiological processes. Individual dosimetry is usually possible and meaningful. A medical physics expert is required. By contrast, special administration techniques are not necessary.

Therapy with open radionuclides, which are injected into preformed cavities in the body, had also become established as early as the 1950s. The most frequently applied form of therapy of this kind today is radiosynoviorthesis (German Commission on Radiological Protection [SSK]; ‘Strahlenschutz bei der Therapie mit Beta-Strahlern in flüssiger Form im Rahmen einer Brachytherapie, Radiosynoviorthese und einer Radioimmuntherapie, Empfehlung der Strahlenschutzkommission, verabschiedet auf der 184. Sitzung der SSK am 31.03./01.04.2003’, Bundesanzeiger; 218; 21 November 2003). Under this approach, open radioactive substances are administered into interarticular spaces in order to treat chronic inflammation. Relatively low activities (usually less than 200 MBq) are handled – in particular if the activity is administered under X-ray control, which is often done outside permanent controlled areas under the Radiation Protection Ordinance (StrlSchV).

Considerably higher activities (typically 2 to 4 GBq Yttrium-90 [\(^{90}\)Y]) are handled in intraperitoneal or intrapleural administration than in radiosynoviorthesis. In principle, the dose is administered in the controlled area of a nuclear medicine therapy ward. Significant contamination of dressing material is possible, and a – small, variable – fraction of the activity administered may be absorbed and excreted, so it is standard for these therapies to be carried out in nuclear medicine therapy wards. The therapies discussed above require little supporting equipment. Individual dosimetry is not possible and also not required. For this reason, these therapies can be carried out as what is known as standard therapies. A medical physics expert is merely required to act in an advisory status when this is done.

In contrast to this, a different approach is required to the two forms of therapy dealt with in the present recommendation, i.e. radionuclide therapy by means of selective intraarterial radiotherapy (SIRT) and intravascular irradiation with open radionuclides, not least on account of their radiological protection aspects:

They involve handling of high activities and also, in particular, of high concentrations of activity. In principle, the activity is administered in an angiography cabinet and therefore, in general, outside a permanent controlled area under the Radiation Protection Ordinance. This therapy is delivered on an individual basis, which means it requires dosimetric planning and, consequently, the direct involvement of a medical physics expert competent in the field. As far as the involved doctors are concerned, the performance of the therapy – except in the rare cases where an individual has the specialist expertise in both fields – requires cooperation between a specialist under the X-Ray Ordinance (RöV) and a specialist under the Radiation Protection Ordinance. The success of the therapy is determined decisively by the cooperation between the persons involved. The objective of this paper is to indicate the points of contact, set out responsibilities and draw attention to the necessary radiological protection measures.
Selective intraarterial radiotherapy (SIRT) – indication and description of the procedure

Selective intraarterial radiotherapy (SIRT) is deployed first and foremost to treat primary or secondary neoformations of the liver. Commercial medical products – with CE certification – for this purpose are available or can be produced in-house. In this treatment, radioactive particles (microspheres) are injected via an arterial catheter and are then deposited in the capillaries of the vascular region supplied by the artery, where they irradiate the immediate surrounding volume. At present, exclusively β-emitters with a mean range of approx. 3 mm in tissue are used (\(^{90}\)Y with a half-life of 2.67 days, \(^{186}\)Re with a half-life of 3.8 days).

As a rule, the activity is administered into one of the liver arteries or their branches, where the necessary locations of the catheter positions for the administration of the activity are determined on the vascular system and the vasculature of the parts that are affected in the liver. When the catheter is correctly positioned, the distribution of particles and, subsequently, the distribution of the radiation dose are directly proportional to the arterial blood supply to the dependent tissue. This is why a considerably higher radiation dose is delivered in well-perfused tumours than in a healthy liver. Apart from known tumours, other (micro)-tumour cells that would not (yet) be picked up by (non-invasive) detection techniques may be present. These too are then irradiated at the same time proportionally to the regional distribution of the microspheres, which depends on the flow of blood. In general, the decision not to target the microspheres into an artery that supplies blood to the tumour – something that could in any case only be given consideration when singular tumours are treated – therefore leads to various advantages. The technical steps involved in the performance of the therapy are made easier, and often it makes them possible at all. The intratumoural distribution of the dose can be foreseen better, and inhomogeneities caused by the administration technique can be avoided. In addition to this, all neoplasia in the liver respectively the lobe of the liver are treated simultaneously, depending on their blood supply.

After a principle indication for therapy has been identified, a digital subtraction angiography is required for the planning of the therapy. In this respect, vessels that potentially pose a risk of an extrahepatic outflow of the therapeutic substance (e.g., a. gastroduodenalis, a. gastrica dextra, a. cystica, etc.) may already be occluded at this point. The decision as to which specific vessels are to be occluded, at what point in time they should be occluded and the actual highly selective probing and embolisation of these hepatofugal vessels is a complex task for which particular expertise in endovascular interventional radiology is a compulsory precondition.

After this, a test administration of a diagnostic radiopharmaceutical (e.g., \(^{99m}\)Tc-MAA\(^1\)) is undertaken in order to examine the regional blood supply conditions, detect extrahepatic concentrations and quantify the hepatopulmonary shunt volume. Since the \(^{99m}\)Tc-MAA examination is intended to simulate the therapy that will later be performed, the position of the catheter for the administration of the \(^{99m}\)Tc-MAA must be stipulated by agreement between a specialist medical doctor under the Radiation Protection Ordinance and a specialist medical doctor under the X-Ray Ordinance. A fraction of the activity finds its way into the venous system as a result of intrahepatic shunts, in particular intratumoural shunts, and is ultimately fixed in the lung. Here, the whole lung undergoes largely homogeneous irradiation. The lung dose can and must be estimated prior to the therapy and may limit the activity that

\(^1\) Technetium-99m-labelled denatured human albumin particles (Technetium-99m-macroaggregated albumin).
can be administered. Furthermore, an extrahepatic intraabdominal fixation of activity must be ruled out or its clinical relevance evaluated. With regard to the occlusion of the vessels discussed above, it is necessary to bear in mind that collaterals may form over time. Following careful consideration of the risks, the therapy should be carried out promptly. In particular, changes in the catheter position should be considered, which could result in a renewed $^{99m}$Tc-MAA investigation.

Prior to the therapy, it is necessary to carry out therapy planning, in which the indication for the therapy is identified, with due consideration of the technical competence of the specialists involved in the performance of the therapy, and the therapeutic concept is stipulated. Not least in view of the application of therapeutic radiation doses, it must be ensured that no tumour is detectable outside the liver, or that the tumours in the liver are decisive for the further course of the patient’s condition. This means a comprehensive prediagnostic examination is requested, with includes latest diagnostic developments.

While the specialist medical doctor under the Radiation Protection Ordinance (as a rule a nuclear medicine expert) is responsible for the planning of the therapy and jointly responsible for its dosimetric aspects with the medical physics expert, the specialist medical doctor under the X-Ray Ordinance (as a rule a radiologist) must take responsibility for that important part of the execution of the therapy that falls within his specialist expertise. It is necessary that a written standard flow chart is drawn up as part of the working instructions, in which the specific competences of the persons involved are recorded. An optimal safety and success of therapy requires a pretherapeutical analysis of all available imaging material and discussion of indication as well as performance of the therapy as a joint approach of the team involved. The therapeutic concept and the treatment plan are to be documented in writing. As a rule, the medical indication has already been clarified in advance at a multidisciplinary tumour meeting. On account of the necessary individual planning of the therapy and its extensive, complex requirements with regard to radiological protection, SIRT may not be performed as an outpatient therapy within the meaning of the Guideline on Radiation Protection in Medicine.

2.1 Recommendations concerning the preparation and performance of the therapy

Prior to a treatment with radioactively labelled microspheres, an angiography is absolutely essential in order to investigate the following aspects:

- Are normal anatomical variants of the arterial vascular network present?
- Is there an adequate antegrade arterial flow into the liver?
- Is a portal vein thrombosis present (if not previously clarified in the cross-sectional diagnostics)?
- What is the arterial perfusion of the tumour like?

After the decision to carry out SIRT has been made, the diagnostic part of the angiography is supplemented with the following measures:

- The coil embolisation of vessels through which any potential extrahepatic outflow could take place, where applicable.
MAA injection to quantify the hepatopulmonary shunt fraction, excludes and, where applicable, assesses the extrahepatic fixation of activity, and assesses and (semi)quantify the tumour blood supply relative to the liver blood supply.

The diagnostic angiography should begin with a survey aortography in order to identify possible normal anatomical variants of the liver vasculature with certainty. If a contrast medium-intensified CT or MRT is already available prior to the angiography or if the vascular conditions are known from previous angiographies, it is possible to omit this survey aortography.

Furthermore, the angiography should include a selective visualisation of the hepatic vascular system. It is compulsory for normal anatomical variants to be documented for the planning of the therapy. In addition, it is necessary to search for possible vascular changes (e.g., stenoses) that may have an influence on hemodynamics. For instance, an adequate antegrade flow of blood into the liver is to be required for SIRT since gastrointestinal complications may otherwise be encouraged due to the retrograde flow of microspheres along the catheter.

The arterial perfusion of the tumour is an important parameter for the success of therapy with radioactive microspheres and is documented either in cross-sectional imaging (CT and/or MRT) or angiographically. Where applicable, it is possible to detect a hypervascularisation of the tumour that would otherwise not be visible using angiography-based flat-panel volumetric CT following administration of a contrast medium via the inserted angiography catheter. The perfusion conditions are checked quantitatively in the course of the $^{99m}$Tc-MAA-SPECT investigation. If no hypervascularisation of the tumour is evident at a preliminary stage, the indication for the therapy must be reviewed critically with radioactively labelled microspheres. Where applicable, an investigation with $^{99m}$Tc-labelled MAA will allow a final decision to be taken.

The preparation of patients for the therapy requires the certain identification of gastrointestinal collaterals that originate from the hepatic circulatory region. After the visualisation of the extrahepatic vessels, these vessels are occluded, in so far as they are located in the region where the therapy will later be performed or close to the microcatheter position from which the therapy is carried out. In this respect, it is necessary to take into consideration that there may be a reversal of the flow in the vascular system under treatment during the injection, in particular due to the embolising effect of particular SIRT preparations. This implies that side vessels that do not supply the liver and clearly branch off from the main vessel proximally to the catheter position are also to be occluded. Gastrointestinal collaterals should be permanently occluded, e.g. using coils.

At the latest 15 minutes before the $^{99m}$Tc-MAA is given, perchlorate is administered orally to the patient once in order to prevent unspecific visualisation of the stomach. Otherwise, the sensitivity with which an extrahepatic abdominal concentration of activity is detected would be reduced.

$^{99m}$Tc-MAA is injected intraarterially via a microcatheter inserted into the angiography catheter. Depending on the anatomy and the extent of the tumour in the liver, $^{99m}$Tc-MAA may be administered by lobar injection via the a. hepatica dextra and/or sinistra. Injections into both lobes of the liver via the a. hepatica propria or communis should only be carried out in exceptional cases; since the risk of extrahepatic nuclide dispersion increases the further the liver is from the point of administration. Territories below a lobe of the liver may also be defined as the target volume, where applicable. If $^{99m}$Tc-MAA is injected into several vessels
in one session, the total activity of approx. 150 MBq should be distributed among these vessels – preferably in proportion to the masses of tissue supplied by the vessels.

The imaging after the $^{99m}$Tc-MAA administration should preferably be undertaken with a combination of functional and morphological imaging (e.g., SPECT/CT), in order to not only facilitate the quantification of the hepatopulmonary shunt volume, but also to morphologically classify any potential extrahepatic outflow. Should a relevant abdominal extrahepatic $^{99m}$Tc-MAA concentration be detectable in the scintigraphy, the corresponding vessel must be identified prior to therapy and, if possible, occluded.

The distribution of the activity from the therapeutic preparation is to be documented posttherapeutically (preferably within 24 hours). In the case of pure β-emitters such as $^{90}$Y, bremsstrahlung images must be generated using instruments with settings optimised for this purpose.

2.1.1 Constructional and organisational radiological protection

There are currently no angiography rooms in Germany that fulfil all the requirements with regard to controlled areas for the handling of open radioactive substances. For this reason, as a rule, the therapy is carried out in temporary controlled areas under the Radiation Protection Ordinance. The radiological protection measures to be observed are stipulated with the competent supervisory authority when the handling license is issued.

If buildings are newly constructed or significant constructional changes are made, an airlock entrance for patients and personnel, and a segregated room for the assembly of the injection facility are to be installed. A closed spatial unit consisting of an airlock entrance, preparation room and angiography room minimises the danger of contamination escaping. As a protective measure against contamination that cannot be completely removed in the room, e.g., a suitable covering is required for the floor.

As far as the requirements with regard to constructional radiological protection are concerned, it should be taken into consideration that, as a general rule, the performance of SIRT only takes up a small proportion of the time this room is in use and the available facilities for applications under the Radiation Protection Ordinance can only be retrofitted imperfectly. Since, in these cases, constructional radiological protection in particular cannot be implemented fully, more demanding requirements with regard to organisational radiological protection are to be imposed.

As far as organisational radiological protection is concerned, the following points are to be heeded, in particular:

- X-ray protective clothing and protection from contamination are absolutely essential for all persons present in the administration room.

- Disposable parts that still contain activity and potentially contaminated objects must be stored and disposed of professionally. These parts may only be transported in suitable shielding or shielded containers.

- The angiography room must be checked after each treatment to ascertain whether it is free of contamination. Measurements to detect contamination must also be carried out on all persons employed in the angiography room and patients. The equipment necessary for decontamination is to be kept on the premises.
2.1.2 Patient protection

The actual therapy is performed via a coaxial catheter system at the previously stipulated location in the hepatic vascular system. It is necessary to visually document the correct positioning of the catheter, in particular immediately before and after the injection, and to carry out repeated controls of the correct antegrade flow of blood, if required. If there are delays in carrying out the injection or it is suspected that the catheter tip may have been dislocated (e.g., by patient movements), the control of the correct positioning of the catheter is to be repeated. Commercially available microspheres are exclusively to be administered using the special administration systems supplied by the manufacturers.

2.1.3 Protection of personnel

As far as the radiation exposure of personnel is concerned, it is necessary to look at different situations and groups: performance of the therapy, nursing on the ward and any possible intervention by means of an operation after therapy.

With regard to radiological protection when the therapy is carried out, it is necessary to observe the manufacturer’s instructions, which will have been reviewed when the preparation was approved. The connection between the administration unit and the patient is not taken into consideration in this respect. The passage of the microspheres through the administration tube may cause relevant radiation exposures of the personnel. Accordingly, protective measures against β-radiation (shielding, distance) are to be taken.

The bremsstrahlung from the patient is of subordinate significance on account of the low dose rate to the nursing personnel. However, it is not possible to rule out that the dressing material or other objects found on the patient are contaminated and, due to the bremsstrahlung emitted by the patient, such objects can only be measured with certainty after their removal from the patient. The patient’s excretions are to be considered to be contaminated until their status has been clarified using appropriate measuring technologies. Nursing care on nuclear medicine therapy wards does not require any additional precautions. Should the patient have to be cared for outside a nuclear medicine therapy ward for health reasons, a temporary controlled area is to be established. In particular, the members of staff who work there must be instructed to check all materials that have been in contact with the patient to ascertain whether they are free of contamination. In cases where contamination is found, the materials must be sent for professional storage or waste management via the nuclear medicine therapy ward. Prior to the revocation of the temporary controlled area designation, it is to be demonstrated that the area is free of contamination.

During the licensing process, it is to be ensured that the license holder disposes of sufficient personnel who possess the necessary experience of handling beta emitters and that the necessary measuring instruments are available.

SIRT may also be deployed as what is termed a bridge therapy for patients who are waiting for a liver transplant. It is therefore not to be ruled out that the liver will be explanted very soon after SIRT. If no protective measures are taken, the surgeon may be irradiated significantly in the course of such an operation. The irradiation results overwhelmingly from the activity in the outermost layer of the liver (approx. the top 3 mm) and affects those of the surgeon’s body parts that are in line-of-sight contact with it – primarily the hands. This is remedied by a shield just a few mm thick (water-equivalent). The radiological protection measures necessary are to be stipulated in advance in each individual case, and the radiation exposure of the surgeon’s hands is to be measured using a suitable finger ring dosimeter. The
exposure depends decisively on whether heavily concentrating tumours are located peripherally on the liver. The possibility of a liver transplant – which will in fact only rarely be undertaken soon after SIRT – should not preclude therapy, and SIRT should also not disqualify the patient from a transplant operation. If a concept for the operation that stipulates suitable measures to minimise radiation exposures is elaborated in cooperation with a medical physics expert, it is possible to guarantee compliance with the limits for personnel set out in the Radiation Protection Ordinance.

Provided there are no medical reasons against it, the activity of the explanted organ should subside until it falls below the clearance value. Otherwise, the medical physics expert involved in the therapy is to be consulted for the planning of further action optimised for the perspective of radiological protection.

3 Intravascular irradiation with open radioactive substances for restenosis prophylaxis after PTA$^{2}$ and PTCA$^{3}$ – description of the procedure

Intravascular brachytherapy is carried out following the dilation of a previously constricted vessel (with or without the implantation of a stent). The objective of the irradiation is to inhibit the proliferation of smooth muscle cells and myofibroblasts around the tunica media and adventitia (middle and outer layers of the artery) of the dilated section of vessel. This should prevent intima hyperproliferation (intima = inner layer of the artery) and constrictive vessel remodelling.

The corresponding section of the vessel is irradiated from the interior of the vessel. In the past, this was done using considerably different methods of irradiation. In this respect, both gamma and beta emitters have been deployed. Irradiation has mostly been performed using encapsulated radioactive substances in the form of wires, ‘seeds’ or ‘trains’, which were centred or uncentred in the vessel, but also by filling balloon catheters with radioactive fluids or gases.

The effectiveness of intravascular irradiation for restenosis prophylaxis after PTA and PTCA has been demonstrated in extensive studies. Despite the good clinical results of intravascular brachytherapy, the introduction of DESs$^{4}$ led to intravascular brachytherapy being almost completely out of the market. However, it has become apparent that DESs are not suitable or not available for many applications (e.g., in-stent restenoses, stenoses in the pelvis-leg area).

In its statement of 7 December 2000 on endovascular radiotherapy, the SSK set itself the task of continuing to address the special radiological protection problems of endovascular radiotherapy if corresponding methods become established in practice. There has been a revival of intravascular irradiation, and an improved balloon catheter irradiation system has been commercially available since 2008.

In this method, a balloon catheter is positioned in a previously dilated section of the vessel and filled with radioactive fluid. This is centred in the lumen of the vessel by filling the

$^{2}$ Percutaneous transluminal angioplasty.
$^{3}$ Percutaneous transluminal coronary angioplasty.
$^{4}$ Drug-eluting stents.
balloon at (low) pressure, and the wall of the vessel is in essence irradiated radially and symmetrically. $^{188}$Re-perrhenate solution is used to fill the balloon. The beta radiation from $^{188}$Re, with its maximum range of approximately 10 mm in tissue, brings about local irradiation of the dilated section of the vessel. In this context, the dose falls sharply with the distance from the catheter surface. Usually, the intention is to deliver a dose between 10 and 20 Gy around the media. In this context, the irradiation time required to reach this dose depends in essence on the distance of the target tissue from the surface of the balloon, the concentration of activity and the diameter of the balloon catheter. The individual dosimetry is to be carried out in close cooperation with a specialist medical physics expert and allows the irradiation time necessary for the therapy to be calculated. For this reason, this therapy fails to satisfy the criteria for performance on an outpatient basis (chapter 6.6.3 of the Guideline on Radiation Protection in Medicine).

In peripheral vessels with a lumen of 4 to 6 mm, the maximum distance from the media to the surface of the balloon is approximately 2 mm; due to the maximum tolerable occlusion time for the vessel, irradiation times of 10 to 20 minutes are possible in this context. In order to comply with these time constraints, a concentration of activity of approximately 5 GBq/ml is required. When intravascular irradiation is applied after PTCA, it is to be taken into consideration that the lumen of the coronary vessels and therefore the distance of the target tissue from the surface of the balloon as well are smaller. However, the tolerable occlusion time and the irradiation time permitted are considerably shorter, so that higher concentrations of activity up to 10 GBq/ml are required. Where applicable, the irradiation time may also be interrupted with the catheter filled several times providing intervening recovery periods (reperfusion periods).

### 3.1 Recommendations concerning the preparation and performance of the therapy

The therapy must be planned in cooperation between a specialist medical doctor under the X-Ray Ordinance and a specialist medical doctor under the Radiation Protection Ordinance. The target volume for the therapy must be defined in advance, and a medical physics expert must check prior to therapy whether the activity or the concentration of activity present is sufficient to achieve the objectives of the therapy.

#### 3.1.1 Constructional and organisational radiological protection

At present, the therapy is in general performed outside a nuclear medicine controlled area. The comments made in section 2.1.1 apply to this method as well. It is not necessary for the patient to receive routine care on a nuclear medicine therapy ward after the therapy. Due to the possibility of contamination, however, it is to be ensured that the patient can be transferred to a nuclear medicine therapy ward at any time.

#### 3.1.2 Patient protection

In normal cases, the patient does not incorporate radioactivity of any kind, as it is sucked out again from the catheter, after which the catheter is removed. However, there can be a leak in the catheter, in which case varying amounts of activity would find their way into the bloodstream. In consequence, a whole body radiation exposure would be obtained. Such events are rare, but not completely to be ruled out. The catheter deployed for dilation may not be used for irradiation; instead, it is necessary to use a separate irradiation catheter, which is filled at a lower pressure of approx. 2 bars, far less than its nominal pressure, which is usually
10 to 20 bar. This further reduces the risk of a rupture. Despite this, an appropriate emergency schedule (see Annex 2) is to be drawn up and organised as part of the working instructions.

It is necessary to estimate in advance what amount of whole body dose or organ doses the patient would receive in case of an incident of this kind. Measures are to be taken that hinder the uptake of potentially released activity in endangered organs (e.g., as a rule a prophylactic blockade of the thyroid gland with perchlorate) and accelerate the excretion of the radioactive substance. The patient must be transferred to a nuclear medicine therapy ward without delay. All excretions are to be collected from the time when the balloon ruptures until the patient’s arrival at the nuclear medicine therapy ward, and all the materials found on the patient (e.g., cellulose, cloths, clothing, etc.) are to be regarded as potentially contaminated.

3.1.3 Protection of personnel

On account of the very high concentration of activity, the dose rate that results from the beta radiation is very high in the immediate proximity of the radioactive substance. For this reason, the beta radiation must be shielded whenever possible. Gripping tools are always to be deployed when equipment filled with radioactivity is handled. Suitable finger-ring dosimeters are to be deployed to measure the hand dose.

Apart from beta radiation, moderately hard gamma radiation (63-155 keV) and hard gamma radiation (450 keV-2 MeV) are emitted from $^{188}$Re, which to some extent means that heavy shielding is required when the activity is handled, transported and stored.

During treatment, the radioactive fluid is kept in a closed system that consists of a storage container, administration syringe, balloon catheter and various accessories. After irradiation, most of the fluid is sucked back into the container. Once it has been withdrawn, the balloon catheter is deposited in a specially shielded container together with the administration syringe and the disposable parts. The whole irradiation system remains unopened. However, it is necessary to detach it from the storage container, and it is in principle possible for contaminations to occur when this is done.

In normal cases, the patient is free of activity and may be transferred to any ward. It is not necessary for the personnel who work there to be given any instruction. In the case of a catheter rupture/leakage or some other contamination of the patient, immediate admission to a nuclear medicine therapy ward is required. The therapy ward must have a license to handle the radionuclide that has been used. Further-reaching requirements with regard to the ward do not need to be defined.

4 Special requirements

The SSK notes that the handling of β-rays at the activities discussed here demands a particularly high level of care. If 1 GBq $^{90}$Y is handled without shielding, the annual limit for skin doses may already be exceeded during just one administration, while deterministic skin damage may even be triggered if the activity vial is held in the hand. The precise value depends heavily on the geometry of the container and the distribution of the fluid. It also needs to be borne in mind that the (unshielded) administration tubes/catheters constitute a strong source of radiation during injection. The range of β-particles may be limited to a few millimeters in tissue, but it is several metres in air. The detection and quantitative measurement of β-radiation presupposes particular instruments and competence. The SSK
therefore recommends that a sufficient number of persons who have experience of handling open β-emitters and the radiological protection problems that occur when this is done must be present.

As a rule, the therapies are delivered in angiography rooms that are controlled areas under the X-Ray Ordinance. For this reason, the SSK recommends that as long as open radioactivity is present in the room, i.e. until the patient has left the room and it has been demonstrated that the room is free of contamination, the room should also be designated a temporary controlled area under the Radiation Protection Ordinance. The handling of open radioactive substances in angiography rooms requires licensing by the competent authority. The functions and responsibilities of the specialists involved must be stipulated in the licensing decision by means of work instructions as provided for in Section 34 of the Radiation Protection Ordinance. The deployment of these therapies in studies requires licensing within the framework laid down by Section 23 of the Radiation Protection Ordinance.

Suitable shielded containers must be available for the handling, transportation and storage of the radioactive substance. The same also applies to the radioactive waste that arises. Objects to which activity is attached may only be handled with suitable gripping tools.

Surfaces at danger of contamination must be covered when the therapy is carried out, e.g. with easily removable foils, at least in an angiography room where there are surfaces that are difficult to decontaminate. After irradiation, the rooms are to be measured professionally to ascertain whether they are free of contamination and the designation as a controlled area under the Radiation Protection Ordinance can be withdrawn. In cases in which there is contamination, suitable decontamination measures must be taken.

Aftercare must be guaranteed for patients who undergo the effects and side effects of radiotherapeutic measures.

4.1 **SIRT**

The SSK notes that, where it is indicated, selective intraarterial radionuclide therapy is a suitable method for the treatment of primary or secondary malignant neoformations of the liver. The methodological approach is largely standardised. The therapy must be planned and performed in close cooperation between a specialist medical doctor under the Radiation Protection Ordinance, a specialist medical doctor under the X-Ray Ordinance and a specialist medical physics expert. In this respect, the specialist medical doctor under the Radiation Protection Ordinance bears responsibility for the indication for therapy with an open radioactive substance, the result of the therapy and aftercare. The specialist medical doctor under the X-Ray Ordinance bears responsibility for the radiological interventional element. As an individual therapy subject to demanding requirements with regard to radiological protection, SIRT may not be performed on an outpatient basis.

The SSK recommends that, due to possible contaminations of the patient and dressing material, irrespective of the nuclide used, the patient must spend at least 48 hours on the nuclear medicine therapy ward after the therapy, provided their health status allows this, given that as a rule they have an advanced tumourous condition. Otherwise, they must be cared for on another ward with the background of a nuclear medicine ward. In the first 48 hours, the radiation protection officers remain responsible for the handling of open radioactive substances. Excretions and materials (e.g., dressings) that have potentially been in contact with bodily fluids must be measured to ascertain whether they are free of contamination and
managed as radioactive wastes, where applicable. Attention must be paid to the quality assurance aspects summarised in Annex 1.

4.2 Intravascular irradiation

In continuation of its statement of 7 December 2000 on endovascular radiotherapy, the SSK notes that intravascular irradiation with open radioactive substances is an established procedure for restenosis prophylaxis after PTA and PTCA.

The SSK recommends that the therapy must be performed in close cooperation between a specialist medical doctor under the X-Ray Ordinance, a specialist medical doctor under the Radiation Protection Ordinance and a specialist medical physics expert. The scheduling of the individual procedures involved in the work and the allocation of functions are to be regulated in radiological protection or work instructions. All relevant irradiation parameters (concentration of activity, balloon catheter used, length of irradiation, dilated section of vessel, dose at defined distance from the surface of the balloon, irradiation time, irradiation fractions) are to be documented in the irradiation planning and documentation. In view of the individual dose planning it involves, the SSK recommends that the performance of this therapy on an outpatient basis not be licensed.

Due to the potential for a rupture of the balloon, something that is admittedly rare, but nevertheless possible, and the risk the patient will incorporate radiation with which this is associated, it must be ensured that the patient can be transferred to a nuclear medicine therapy ward immediately after incorporating any radiation. There must be an emergency plan for cases of this kind tailored to the situation of the therapy unit (for an example that illustrates these general points, see Annex 2).

In order to reduce the risk of a balloon rupture, the catheter deployed for dilation is not to be used for irradiation; instead, it is necessary to use a separate irradiation catheter, which is filled at a pressure far below its nominal pressure. Furthermore, the irradiation catheter is to be checked for leaks immediately prior to the irradiation.
ANNEX 1

Quality assurance aspects with regard to SIRT

The specialist medical doctor under the Radiation Protection Ordinance who is responsible must be personally present during the administration of the activity. They will have previously discussed the therapeutic concept with the specialist medical doctor under the X-Ray Ordinance. The activity is administered after the specialist medical doctor under the X-Ray Ordinance has demonstrated to the specialist medical doctor under the Radiation Protection Ordinance that the catheter tip is in the desired position and the latter has explicitly approved administration. The person who performs the technical steps involved in administration depends on the individual circumstances. The specialist medical doctor under the Radiation Protection Ordinance is also responsible for the technical element of the administration procedure. A medical physics expert is present during administration in order to control the dosimetry and compliance with safety measures, and subsequently for contamination controls, decontamination measures and waste management.

Dose rate measuring instruments are positioned on the therapy apparatus in order to display the transfer of activity (or residual activities) from the activity vial into the microcatheter.

Only specially qualified personnel are allowed to perform the therapy after in-depth training (practical training). In particular, any persons involved who do not have a nuclear medical background must be informed about radiological protection aspects when β-emitters are handled. In addition to this, the specialist medical doctor under the X-Ray Ordinance (interventional radiologist) must be instructed about the theoretical background of the therapy, and they must be aware that the position of the tip of the administration catheter is just as decisive for the therapy as the even, thorough mixing of the therapeutic particles with the flow of blood. The same is true of the radiological volumetry of the part of the liver or tumour to be treated and the reliability of the catheter tip positioning.

Apart from further theoretical instruction, practical training and routine application, the training also encompasses training for non-routine procedures, including the premature discontinuation of administration (or leakage): termination of injection, separation of the patient from the system, disposal of all system components, including the activity vial, administration set, catheter, documents, gloves, etc., in shielded waste containers, contamination control of all persons who leave the room, decontamination of the room and checks to ascertain whether it is free of contamination.

The activity must be determined with two independent measurement procedures.

Activimeters must be specially calibrated to the containers used (material, wall thickness, geometry, contents). Otherwise, it is possible for the measurements to be incorrect by 50 % or more.

Constant monitoring of the dose rate/progression of activity levels on the administration route (to ensure complete administration, immediately identify residual activities).

Control of the assembly and of the procedure using checklists, inspection by a second person.

In cases where there is contamination, it is to be borne in mind that the activity is bound to corpuscles, i.e. discretely distributed. There must be suitable decontamination equipment in the facility that makes it possible to remove these microscopic particles. Repeated ‘dilution’,...
as when fluids are decontaminated, does not lead to success with any degree of certainty; e.g., it is possible to work with self-adhesive foils that ‘rip off’ the top layer of the floor.

**Literature for Annex 1**


ANNEX 2

Emergency scheme for the rupture of a PTA balloon filled with a β-emitter (illustrated by the example of a balloon filled with $^{188}$Re-perrhenate)

Rationale

$^{188}$Re is a beta emitter. In its pharmacological form, perrhenate, it is mainly absorbed by the thyroid gland cells and parietal cells of the stomach, and excreted renally. In order to reduce the radiation exposure of these organs in cases when activity escapes due to the rupture of an intravascularly inserted balloon, the absorption of the perrhenate into the above-mentioned cells may be blocked by perchlorate and its excretion accelerated by forced diuresis.

Immediate measures

- Deflate balloon
- Evacuate catheter.

Medicinal intervention

- Blockade of the thyroid gland and the parietal cells of the stomach with perchlorate:
  e.g. 40 drops (600 mg) perchlorate (Irenat$^R$) immediately, followed by e.g. 3 x 40 drops (900 mg) over two days.
- Forced diuresis:
  e.g. infusion with 4 (kidney failure) to 6 (healthy kidneys) litres of Ringer’s solution with 10 (healthy kidneys) to 20 (kidney failure) mg Furosemide/l over 2 days (the distinction between healthy and failing is drawn at 1.5 mg/dl creatinine), maximum infusion speed 4 mg/min (perfusor).
- Insertion of a bladder catheter to reduce radiation exposure of the urinary bladder wall.

Control investigations

- Fluid balance, additional infusions where applicable.
- Electrolyte controls, substitution (above all potassium!) where applicable.
- Pay attention for signs of cardiac failure!
- Control glucose level.

For radiological protection reasons, the patient must be admitted to a nuclear medicine ward that has a corresponding handling license for at least 48 hours for monitoring and the measures necessary to reduce radiation exposure. In so far as the specialist medical doctor under the Radiation Protection Ordinance responsible for the treatment does not have such a ward at their disposal, a cooperation agreement must be concluded contractually with a ward on which it is ensured that a patient will be admitted at any time in an emergency.
Literature for Annex 2


