This brochure describes the various pulmonological interventions in the lung supported by Erbe technology. The Erbe pulmonology workstation, which combines the units for electrosurgery, APC (argon plasma coagulation), and cryosurgery on one cart, forms the basis. Flexible cryoprobes can be used, for example, for diagnostic tissue biopsies and tumor extraction. Flexible monopolar instruments can be used to devitalize tissue and control bleeding.
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Our Pulmonology workstation consists of an electrosurgical unit with an APC module and the ERBECRYO® 2. Together, they form the basis for various applications in interventional pulmonology. The systems can also be kept on separate carts, as necessary.

The electrosurgical unit, e.g. the VIO® 3, generates the high-frequency current necessary for flexible monopolar applications and makes it available in various modes. It is also the master unit that controls the APC module, e.g. the APC 3 in this case. This module controls the flow of the argon gas for the argon plasma coagulation (APC) non-contact procedure. The ERBECRYO® 2 controls the CO₂ gas flow for the flexible cryoprobes.

The Erbe pulmonology workstation supports the use of different monopolar instruments and flexible cryoprobes for interventional pulmonology.
**OPERATING PRINCIPLE OF CRYOTECHNIQUES**

The freezing effect of the ERBECRYO® 2 is based on the Joule-Thomson effect: The relaxation (decompression) of certain gases at room temperature, e.g. carbon dioxide, gathers energy from the surrounding area and cools it down. The physical freezing temperature of CO₂ is -78.5°C. However, this is a theoretical value that can be reduced through system characteristics.

**FUNCTIONALITY OF THE PROBE**

The carbon dioxide flows with high pressure from the gas cylinder to the cryoprobe via the cryosurgical unit. Here, it is conducted via a narrow tube to the hollow tip of the probe. Here the gas enters the probe tip via a nozzle. The gas decompresses during influx due to the large pressure difference between the high-pressure tube and the interior of the probe tip. Here, the Joule-Thomson-Effect very rapidly cools down the tip of the probe. Based on different influencing factors, e.g. cylinder pressure or probe size, temperatures between -35°C and -50°C are possible at the tip of the flexible cryoprobes.

The decompressed gas flows through the probe back to the unit and from there into the surrounding area.
Tissue effects of flexible cryoprobes

Upon activation, the ice-cold probe tip enables cryoadhesion and cryodevitalization.

CRYOADHESION

Cryoadhesion is used in interventional pulmonology, for example, to recanalize tumors, collect tissue biopsies, and extract foreign bodies, blood clots, and mucous plugs.

A requirement of the adhesion effect is fluid between the tip of the cryo-probe and the target to be extracted (e.g., foreign body, tissue, blood clot or mucous plug). Once this fluid freezes by the cooling effect of the probe tip, the tip is joined to the object via the formation of ice crystals.

The size of the frozen area has a direct effect on the size of the collected tissue samples. It depends on the following factors:

1. **Freeze time**: The longer the freezing process lasts, the more extensive the frozen area becomes on the target tissue or foreign body to be extracted. The frozen area expands rapidly for up to 5 seconds, after which it expands more slowly. From approx. 10 seconds onward, the frozen area only expands very slowly because a thermal equilibrium develops as the heat dissipates and the frozen area isolates the probe tip.

2. **Contact area**: The diameter of the probe is a major influencing factor on the freezing result. The larger the surface area of the active cryoprobe head, the greater the freezing effect per unit of time.

3. **Moisture**: Moisture is required to connect the cryoprobe with the target. The cryoeffect may be reduced if there is too little moisture.

4. **Tissue and foreign body properties**: The properties of the tissue or foreign body have an influence on the cryoeffect. Materials that are organic, soft, and contain water, such as tissue and food, tend to adhere better than hard, smooth, and inorganic materials, such as plastic or metal.

5. **Cylinder pressure and ambient temperature**: The ambient temperature has a direct influence on the cylinder pressure because the temperature of the liquid carbon dioxide correlates with its evaporation pressure. If it is too high, the ERBECRYO® 2 can compensate for this up to 75 bar. The pressure in the gas cylinder has an influence on the cryoeffect. If it is too low, the ERBECRYO® 2 is unable to compensate for this and will lose freeze performance. The ERBECRYO® 2 will notify the user to this effect.
Cryoprobe is used in interventional pulmonology with the aim to freeze and devitalize tissue. Cold leads to crystallization of intracellular and extracellular fluid. The cell walls are destroyed through the formation of crystals and recrystallization during the thawing process, thus enabling tissue devitalization.

The following factors influence the efficacy of tissue cryodevitalization:

1. **Low freezing temperature:** A potential devitalization of various tissues starts at -10°C. A temperature below -35°C is sufficient for the effective devitalization of most tumor types.8

2. **Cooling rate:** The faster the cooling, the more effective the intracellular formation of crystals and thus devitalization. At -10°C to -50°C/min, the intracellular formation of ice crystals is enhanced and thus provides for cell devitalization. The cooling rate of the flexible cryoprobes is over -1,500°C/min and thus more than adequate.6

3. **Repetition of freezing and thawing cycles:** Multiple freezing and thawing cycles at the same spot support effective devitalization. Studies have found that a complete devitalization of tumor tissue is enhanced using two cycles or more.8

4. **Freeze time:** „The longer, the better“ is not necessarily true for devitalization. Studies have found that as little as 20 seconds are sufficient to destroy cells through intracellular formation of ice crystals. In pulmonology, between 20 seconds and 3 minutes are used.9,10,11

5. **Thawing rate:** If biological tissue thaws slowly, extracellular recrystallization occurs as well as a change of the extra- and intracellular physiological concentration of saline solution, which contribute to osmotic cell lysis. Therefore, the slowest possible thawing phase, e.g. through passive thawing, is recommended.8
Flexible cryoprobes

Flexible cryoprobes can be used for various clinical applications, for example, to devitalize tissue and to extract foreign bodies, mucous plugs, blood clots, necrotic tissue, tissue tumors (recanalization), and tissue biopsies.\(^2\)

Single-use cryoprobes are available with diameters of 1.1 mm, 1.7 mm and 2.4 mm.

All three probes are suitable for use with bronchoscopes of corresponding sizes and the 1.1 mm and 1.7 mm probes are compatible with navigation catheters by different manufacturers.

In addition to the single-use cryoprobes, we also offer reusable cryoprobes with a diameter of 1.9 mm and 2.4 mm.
In addition, the 1.1 mm cryoprobe allows biopsies to be recovered through the working channel of a bronchoscope, just like with a flexible forceps. The oversheath used during this procedure protects the tissue sample and the bronchoscope.12

In addition, the probe is compatible with bronchoscopes with a 1.2 mm working channel and enables biopsies through various navigation catheters.
Flexible cryoprobes enable many different applications in interventional pulmonology. Typical applications include cryoextractions, such as tumor removal, tissue biopsy collection, extraction of foreign bodies, blood clots, and mucous plugs, and cryodevitalization. For cryoextractions, the larger flexible cryoprobes (OD 1.7 mm, 1.9 mm or 2.4 mm) must be removed together with the bronchoscope or guiding catheter. This is because the pieces of tissue or foreign bodies are too large for the working channel of the bronchoscope or guiding system.\(^3\)

Conversely, the thin 1.1 mm cryoprobe with oversheath enables the collection of tissue samples through the working channel of a therapeutic bronchoscope with a 2.8 mm working channel.

**Biopsy sampling**

Cryoadhesion with flexible cryoprobes enables the extraction of biopsies from the central and peripheral regions of the lung.\(^6\)

---

**ENDOBRONCHIAL CRYOBIOPSIES**

Endobronchial cryobiopsies have now become a recognized and established biopsy procedure in interventional bronchoscopy and are mentioned in various guidelines. The procedure has shown to be safe and effective in studies.\(^16\)

**Described diagnoses**

The following benign and malignant indications are described for endobronchial biopsy sampling using flexible cryoprobes:\(^17,18\)

- Lung cancer
- Metastatic colon adenocarcinoma
- Sarcoma
- Lymphoma
- Squamous cell carcinoma
- Mucoepidermoid carcinoma
- Metastatic renal cell carcinoma
- Endobronchial tuberculosis
- Non-tuberculous granuloma
- Leiomyoma
- Chondroma
- Carcinoid
- Clear cell carcinoma
- Cystic adenocarcinoma
- Adenocarcinoma
In order to extract an endobronchial cryobiopsy, the tip of the cryoprobe is frozen to the target tissue in the bronchial system. Once the desired freeze time has elapsed, the cryoprobe is withdrawn abruptly together with the bronchoscope. The biopsy detaches from the cell group and can be removed together with the probe and bronchoscope. Described freeze times vary between 2 and 5 seconds.³,¹⁰

**Important technical information:**
The freezing process with the ERBECRYO® 2 is interrupted as soon as the activation is stopped with the footswitch. Therefore, it is important that activation with the ERBECRYO® 2 is maintained until the tissue sample has been completely extracted from the patient.

The tissue sample is carefully detached from the tip of the cryoprobe after thawing it, e.g. in physiological saline solution. The cryoprobe can then be removed from the working channel in order to return to the intervention site.

The freezing process can be monitored and controlled visually in the central airways.³

**Clinical results**
Cryobiopsy is commonly evaluated in comparison with conventional mechanical forceps biopsy. In the analyzed studies, cryobiopsy is superior to forceps biopsy.¹⁶

This superiority is demonstrated in the diagnostic yield. While the yield for endobronchial forceps biopsies varies between 59.9% and 85.1%, the yield for endobronchial cryobiopsies is between 81.4% and 100%.¹⁶

This superiority is mainly due to:¹,¹⁶
- Larger tissue samples
- No or fewer crush artifacts
- Tangential applications¹⁶

**Safety**
Complications described for endobronchial cryobiopsies include bleeding. Rates for severe bleeding after cryobiopsies vary between 0.3% and 18.2%¹⁶ with no significant differences for severe bleeding compared to forceps biopsies. For minor and moderate bleeding the rate associated with endobronchial cryobiopsies is increased compared to forceps biopsies.³

The cryoprobe with oversheath supports a safe application. With this system, biopsies can be extracted through the working channel of a bronchoscope, while leaving the bronchoscope in the target area. This enables the bronchoscopist to maintain visual control of the intervention area during the application.²⁰
Applications

TRANSBRONCHIAL CRYOBIOPSIES

Like endobronchial cryobiopsies, transbronchial cryobiopsies have also become a known diagnostic procedure. More than 160 publications on this topic (as of November 2018) demonstrate the high level of scientific activity in this application. Transbronchial cryobiopsies are mainly used to diagnose interstitial lung diseases and peripheral pulmonary nodules.16

Technique

Transbronchial cryobiopsies from the lung periphery are described in different ways. The procedure described here is based on Hetzel et al. 201821: “Transbronchial Cryobiopsies for the Diagnosis of Diffuse Parenchymal Lung Diseases: Expert Statement from the Cryobiopsy Working Group on Safety and Utility and a Call for Standardization of the Procedure”.

This group recommends performing transbronchial cryobiopsies in intubated patients under general anesthesia or deep sedation; spontaneous breathing and jet ventilation are possible.

The cryoprobe should be positioned as closely as possible to the visceral pleura, but no closer than one centimeter because this can increase the risk of pneumothorax. A transbronchial cryobiopsy from the medial third of the lung should be avoided because this can increase the risk of bleeding from unprotected medium-sized blood vessels. In order to achieve the best possible positioning, the biopsy should be performed under fluoroscopic guidance by carefully advancing the cryoprobe to the visceral pleura and then retracting it by one centimeter.

The use of a therapeutic bronchoscope is recommended in order to provide for the greatest possible suction capacity in case of hemorrhage. It also enables a more careful positioning of the cryoprobe because the resistance in the bronchoscope is low.

Probes with a diameter of 1.9 mm and 2.4 mm are described for this application. The freeze time must be individually adjusted based on different variables, but is specified for use with carbon dioxide as follows: 1.9 mm, 7 seconds; 2.4 mm, 5 seconds.

There is no exact recommendation for the optimal number of biopsies for ILD diagnosis, however most studies describe 3-5 biopsies. It is also advised that the diagnostic value for DPLD (Diffuse Parenchymal Lung Disease) can be improved if the biopsies are collected from different segments.

In order to increase the safety of the application, the authors recommend the prophylactic use of a Fogarty catheter in the segment where the biopsy is performed. Especially in the case of flexible intubation because it may not be possible to tamponade quickly enough, if necessary.

In addition, a fluoroscopic check after the intervention is recommended in order to determine a possible pneumothorax.21

Transbronchial cryobiopsy under fluoroscopic guidance

12
Clinical results

Studies show that transbronchial cryobiopsies are larger and qualitatively better than forceps biopsies. This has been studied for interstitial lung diseases and peripheral biopsies for the diagnosis of pulmonary nodules.\textsuperscript{16}

The diagnosis of interstitial lung diseases is the most commonly described application for transbronchial cryobiopsies. In the studies analyzed by Hetzel et al., the diagnostic yield for DPLD is between 50.6\% and 100\%.\textsuperscript{21} By comparison, the diagnostic yield for forceps biopsies is between 25\% and 65\% in the studies in the considered studies.

In the ATS Guideline published in 2018, the authors describe a diagnostic yield of 36.1\% for forceps biopsies for the diagnosis of interstitial pulmonary fibrosis. For transbronchial cryobiopsies, the yield was 80\%, enabling surgical biopsies to be potentially avoided in 80\% of cases, according to the authors. In comparison with surgical biopsy, the authors attribute cryobiopsy with a lower rate of respiratory infections and a trend toward a lower procedural mortality rate.\textsuperscript{22}

Like forceps biopsy, cryobiopsy is neither recommended nor rejected for the diagnosis of IPF. Raghu et al. describe a yield (definitive diagnosis) of 89\% for surgical lung biopsies in ILD patients.\textsuperscript{22}

Safety

The complications described for transbronchial cryobiopsies include pneumothorax and bleeding. The likelihood of occurrence varies greatly and has been stated by Hetzel et al. 2018\textsuperscript{21} for pneumothorax, major hemorrhage and mortality: Pneumothorax was found in 0–26\% of cases in the analyzed data.\textsuperscript{21} Other analyses found an average of 13.4\%.\textsuperscript{22} Casoni et al. describe a pneumothorax rate of 28\%. The authors cited the patient group and a learning curve to explain this rate.\textsuperscript{23} Major hemorrhage varies between 0.7\%\textsuperscript{22} and 4.3\% (48/1130)\textsuperscript{21} across multiple reviewed studies. The application-related mortality rate is described as 0.2\% [Raghu et al. (1/427)/ Hetzel et al. (1/513)].\textsuperscript{21,22}

Raghu et al. also describe infections in 0.7\% of reviewed cases.\textsuperscript{22} As in the case of surgical biopsy and forceps biopsy, Raghu et al. do not recommend transbronchial cryobiopsy for diagnosis in patients with expected idiopathic pulmonary fibrosis if there is a high-resolution CT with UIP pattern.\textsuperscript{22}

Transbronchial cryobiopsy is generally classified as a safe and effective procedure.\textsuperscript{16}
Applications

CRYORECANALIZATION OF EXOPHYTIC TUMORS

Cryoadhesion is used during cryorecanalization in order to freeze the target tissue to the flexible cryoprobe and then extract it together with the bronchoscope. Corresponding studies describe the recanalization of benign as well as malignant tumors.\textsuperscript{16} Indications for cryorecanalization are endoluminal exophytic tumors or mixed tumors, where combining the technique with stents can be helpful.\textsuperscript{2}

Technique
Cryorecanalization is described with rigid and flexible intubation.

Schumann et al. 2010 describe the following procedure for cryorecanalization:\textsuperscript{2}
1. Introduce the cryoprobe through a flexible or rigid bronchoscope.
2. Place the tip of the cryoprobe on the tumor mass or carefully push it into the tumor mass.
3. Start the freezing process and continue it for 3-5 seconds.
4. Abruptly remove the bronchoscope together with the cryoprobe and the tumor or tumor tissue.
5. Thaw the cryoprobe tip with the extracted tissue in the water bath.
6. Repeat application until the exophytic tumor mass has been re-

Potential learning effects improve the success rate.\textsuperscript{2}

Clinical results
The rate for successful recanalizations of malignant tumors is up to 91.1 \%; other studies report rates from 72.5 \% to 83 \%.\textsuperscript{16,24,25}

The procedures performed for recanalization are described as successful for the respectively performed applications with immediate treatment success in one session.\textsuperscript{16}

Recanalized tumors include adenocarcinoma, adenoid cystic carcinoma, squamous cell carcinoma, hamartoma, non-small cell lung cancer, small cell lung cancer, bronchial metastasis of cervical carcinoma, metastatic renal cell carcinoma, metastatic colon carcinoma, bronchial carcinoid, malignant lymphoma.\textsuperscript{2,24,25}

Safety
Described complications include bleeding which was treated conservatively or with argon plasma coagulation.\textsuperscript{16} The hemorrhage rate was 12 \% with minor hemorrhages in 4 \% and moderate hemorrhages in 8 \% of the cases. In addition, the authors report a perforation of the pars membranacea that was able to be controlled with the administration of antibiotics.\textsuperscript{16}
Hetzel et al. recommend having rigid intubation available in the case of hemorrhage.

Yilmaz et al. report a restenosis rate of 12.8 \%.\textsuperscript{24}

A major advantage of cryorecanalization compared to other procedures, such as laser for example, is that cryorecanalization does not require reduction of oxygen and thus involves no risk of hypoxia.\textsuperscript{23}
The first cryodevitalizations were successfully performed by James Arnott (1797–1883) in the 19th century with a combination of ice and salt. Cryodevitalization has since been further developed and is now widely used for various indications in medicine. 8

Flexible cryoprobes are suitable for tissue devitalization of lung tumors. Unlike APC, laser, and electrosurgery, cryodevitalization only has a minor immediate effect. The greatest effect occurs hours or days later. 26

Cryodevitalization has different advantages. The application is safe even at oxygen concentrations above 40 %.32,27,35,40, damage to the bronchial walls is minor, and there is less pain under local anesthesia.26

Cryosensitive tissue includes skin, nerve, endothelial, granulation, and mucosal tissue.

Cryoresistant tissue includes connective tissue, fibrotic tissue, nerve sheaths, fatty tissue, and cartilage.26,11

Due to the levels of cryoresistant tissue in the bronchial walls, there is almost no risk of a perforation with cryodevitalization.11

Technique
The procedures described by Lee et al. vary from freezing for 1 minute during one to three freezing and thawing cycles to applying up to two activation cycles of 3 minutes each.11

Other authors describe three cycles of 20 to 60 seconds each with a passive thawing process.9,15 According to various sources, cryosensitivity depends on the tissue, which is why the cryospecific parameters of the application must be defined by tissue type.8

The devitalized tissue is then either expectorated or mechanically removed during another bronchoscopic procedure, e.g. with a flexible forceps, several days following devitalization.10,16

Clinical results
In 2011, Lee et al. reviewed the safety and efficacy of cryotherapy of endobronchial tumors. A total of 16 publications were included in the systematic evaluation. The treated indications included lung cancer, carcinoids, benign tumors, lymphoma, melanoma. Most of the treated patients were inoperable. The mean success rate for recanalization using cryodevitalization was 80 %.11

Safety
Complications included hemorrhage, fever, mediastinal emphysema, pneumothorax, and atrial fibrillation. They vary by publication and are reported to be 11.1 % across 10 reviewed studies. In 5 of the studies, mortality occurred in 7.1 % of cases within 30 days of the operation. However, it was considered that most of the mortality was more likely to be associated with disease progression rather than a direct consequence of cryotechniques. The relapse rates were between 11.1 % at 2 years and 28 % at 13–45 months.11

In their overview, Lee et al. reach the conclusion that cryotherapy performed for endobronchial tumors is a safe and effective treatment method. It improves the symptoms, pulmonary function, and performance in patients with endobronchial obstruction, especially in inoperable cases.

Various sources point out that cryodevitalization is not suitable for patients with life-threatening airway obstructions due to its delayed effect.11,37
Applications

REMOVAL OF FOREIGN BODIES, BLOOD CLOTS, AND MUCOUS PLUGS

Cryoadhesion can be used to freeze foreign bodies, blood clots, and mucous plugs to the cryoprobe and extract them together with the bronchoscope. The rule that moist materials are easier to extract with cryoadhesion than dry materials is also applicable here. Moistening the material to be extracted may assist in improving adhesion.

Technique
The application for foreign bodies, blood clots, and mucous plugs is comparable to other cryoextraction methods, such as biopsy or recanalization. Extraction is performed through cryoadhesion and removal of the bronchoscope, including cryoprobe and target material. Freeze times vary quite a bit and are reported at 3 to 5 seconds for foreign bodies. Longer freeze times of 10 to 15 seconds are required for blood clots.

Clinical results
Ex vivo studies have found that cryoextraction is suitable for:
- Organic materials, such as chicken bones and fish bones
- Beans and peas
- Tablets
- Inorganic materials, such as hairpins, staples, and paper clips

In vivo studies describe the successful extraction of:
- Toys
- Teeth
- Chewing gum

Sriratanaviriyakul describes successful extraction in 84.2% of cases:
- 24/26 (92%) for blood clots
- 4/6 (66.67%) for mucous plugs
- 2/4 (50%) for foreign bodies
- 2/2 (100%) for plastic bronchitis

Safety
Studies on foreign body removal with flexible cryoprobes in adults describe the procedure as feasible and safe. In the case of cryoextraction of foreign bodies in children, the results are subject to controversy due to the elevated complication rates. The rates in the study by Zhang et al. on a group of 12 patients included 25% for hemorrhage and 17% for granulation tissue. Hammer et al. refer to the ATS and ERS recommendation for rigid intubation in children for the extraction of foreign bodies and underscore its importance. The authors conclude that the rigid technique in conjunction with mechanical removal is best suited for the extraction of foreign bodies in children.
The indications for electrosurgery in interventional pulmonology include, for example, palliative treatment of malignant tumors of the airways or treatment of benign airway obstructions.26

The application of endobronchial electrocautery was first described by Gilfoy in 1932.32 With the development of the flexible monopolar technique, electrosurgery has been more widely discussed in the field of interventional pulmonology since the 1980s. Its rising popularity can also be attributed to its wide availability and relatively low costs.26

This section describes the contact procedures, in which direct contact is necessary between the application element and the target tissue. The electrosurgical non-contact procedure of argon plasma coagulation (APC) is described in detail in the next section.
Electrosurgery

**Electrosurgical technique**

**MONOPOLAR TECHNIQUE**

In monopolar electrosurgery, current ($I_{mp}$) flows in a closed loop, from
the unit to the instrument, then through the patient’s body to the return
electrode (RE), and finally from the return electrode back to the unit.
The tissue effect occurs at the contact point between the monopolar
instrument and the target tissue. This very small contact area results in
a very high current density, which in turn generates the desired thermal
tissue effect. Thus, for example, an incision or a coagulation can be per-
formed, depending on the generator setting. The return electrode (NE),
has a large surface area and is placed against the patient’s skin at an
appropriate location in order to discharge the current. The increase in
temperature on the large surface of the return electrode is not significant
due to the low current density.

Monopolar electrosurgery can be applied in the case of malignant or
benign diseases.33
Tissue effects in electrosurgery

The two electrosurgical tissue effects of the monopolar technique include cutting and coagulation. The terms are internationally standardized and uniformly used with available electrosurgical units. Cutting is symbolized by yellow activation elements (e.g. footswitch) and coagulation is symbolized by blue activation elements.

**COAGULATION**

Coagulation current can be used to control bleeding, devitalize tissue, and recanalize tumors.

Heat is produced when electrical energy is converted in the tissue. Cell damage is irreversible at temperatures above 50°C to 60°C. The denaturation of proteins and heating of connective tissue cause a shrinkage effect, which is further reinforced by drying of the tissue and evaporation of tissue fluid.

Different tissue effects are achieved, depending on the generator setting.

**CUTTING**

Temperatures of 100°C and higher are used in the cutting modes. Intracellular and extracellular fluids vaporize so quickly that the cell membranes and cell formation rupture and the tissue can be sectioned or cut. At voltages of 200 V and up, sparks ignite between electrode and tissue, enabling the tissue to be cut with no considerable resistance. Cutting currents with different characteristics can be used, depending on the generator setting. See also section on electrosurgical modes.
The heating of the tissue by the electrical current flow leads to different tissue effects depending on the temperature reached.

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<tr>
<th>THERMAL EFFECTS ON BIOLOGICAL TISSUE</th>
<th>Temperature</th>
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<tbody>
<tr>
<td>None</td>
<td>37°C-40°C</td>
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<tr>
<td><strong>Hyperthermia</strong></td>
<td>From ~ 40°C</td>
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<tr>
<td>Initial tissue damage, edema formation, depending on the duration of application, the tissue can recover or die (devitalization)</td>
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<tr>
<td><strong>Devitalization</strong></td>
<td>From ~ 60°C</td>
</tr>
<tr>
<td>of the cells, shrinkage of the connective tissue through denaturation with simultaneous hemostasis</td>
<td></td>
</tr>
<tr>
<td><strong>Coagulation/Desiccation</strong></td>
<td>~ 100°C</td>
</tr>
<tr>
<td>Vaporization of the tissue fluid, depending on the speed of vaporization:</td>
<td></td>
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<tr>
<td>→ Tissue shrinkage and tumor reduction through desiccation (drying out)</td>
<td></td>
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<tr>
<td>or</td>
<td></td>
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<tr>
<td>→ Cutting due to mechanical tearing of the tissue</td>
<td></td>
</tr>
<tr>
<td><strong>Carbonization</strong></td>
<td>From ~ 150°C</td>
</tr>
<tr>
<td>The tissue burns and turns black</td>
<td></td>
</tr>
<tr>
<td><strong>Vaporization</strong></td>
<td>From ~ 300°C</td>
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<tr>
<td>Tissue vaporizes due to extreme heat</td>
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Electrosurgical cutting and coagulation modes

Electrosurgical units provide various modes for flexible monopolar instruments in interventional pulmonology. We describe below the modes of our VIO® 3 electrosurgical unit that are relevant for interventional pulmonology.

**endoCUT® cutting mode**

The endoCUT® cutting mode fractionates the cutting process into cutting and coagulation intervals. Here, the tissue is coagulated at and after each cut. The cutting and coagulation cycles can be adjusted individually to minimize bleeding during bronchoscopic incision.

**Possible endoCUT® mode settings include the following:**

- **Effect:** The effect levels control coagulation between cutting cycles. Greater coagulation is generated with higher effects (e.g. Effect 3) than with lower effects (e.g. Effect 1).
- **Cutting duration:** The cutting duration defines the length of the cut for each cutting cycle. A cutting duration 3 generates a longer cut than a cutting duration 1.
- **Cutting interval:** The cutting interval controls the frequency of cuts per unit of time. The higher the interval setting, the more frequently the incisions per unit of time.

**endoCUT® Q**

endoCUT® Q is suitable for use with flexible snares as well as flexible needle knives. The mode has a high voltage to generate the greatest hemostasis possible while cutting. This makes it suitable for applications requiring maximum control of bleeding.

**endoCUT® I**

The endoCUT® I operating principle is comparable to that of the endoCUT® Q, however, the endoCUT® I has a somewhat lower voltage and thus a somewhat lower hemostatic effect. This enables an incision with less lateral tissue damage.
Coagulation modes

Coagulation modes are used with monopolar forceps or coagulation probes. Like the cutting modes, they require direct contact between the application element and the target tissue. It is described that this results in higher cleaning efforts and a potential loss of efficacy in the case of bleeding. Non-contact methods, such as APC, have the advantage that no adhesion occurs and the instrument does not stick to the target tissue.

**softCOAG®**

softCOAG® is suitable for coagulation of minor bleedings with a maximum application time of 1 to 2 seconds. The mode is also used to treat airway obstructions. softCOAG® enables a slow, deep coagulation and de-vitalization without carbonization of the tissue and without spark formation. Adhesion of the instrument is reduced. The activatable autostop function enables an automatic stop, once successful coagulation and desiccation have been achieved.

**forcedCOAG®**

forcedCOAG® is suitable, for example, for the reduction of exophytic tumors. This coagulation mode provides fast and effective standard coagulation with medium thermal penetration depth. However, an increase in adhesion effects can result from the formation of sparks.

**Difference between softCOAG® and forcedCOAG®**

softCOAG® and forcedCOAG® differ in their tissue effects. The softCOAG® mode generates a slower coagulation with greater depth effect and limited desiccation properties. forcedCOAG® is the opposite: rapid coagulation with good desiccation properties, are accompanied by less depth effect.

The non-contact procedure of argon plasma coagulation is an alternative to forcedCOAG® with its low penetration depth. Adhesion effects can be avoided here.
Flexible electrosurgical instruments

SNARES
Electrosurgical resection with snares is suitable for exophytic, pedunculated lesions. The cutting and coagulating effect of the endoCUT® Q-mode is advantageous for this application. The resected tissue can be histologically evaluated.

NEEDLE KNIVES
Needle knives are suitable, for example, for incise benign, fibrotic, web-like stenoses. Among these instruments, the fractionated cutting process of the endoCUT® can be used.

MONOPOLAR FORCEPS
Monopolar forceps can be used, for example, to control bleeding through coagulation with softCOAG® or forcedCOAG®. Another possible application is the so-called „hot biopsy“, where tissue is extracted using the coagulation current in order to prevent bleeding.

COAGULATION PROBES
Flexible coagulation probes are suitable for contact coagulation with the softCOAG® and forcedCOAG® modes. The penetration depth and coagulation speed can be adapted based on the selected mode.
Electrosurgical applications in pulmonology

Flexible monopolar instruments allow tumor recanalization and bleeding management within electrosurgery.

**TUMOR RECANALIZATION**

Indications for electrosurgery include the treatment of endobronchial malignant or benign tumors or post-intubation stenosis. Electrosurgery is often used as an umbrella term for the use of various monopolar instruments.

Unlike with cryodevitalization, photodynamic therapy or brachytherapy, an immediate effect is achievable with electrosurgery in order to reopen the airway. Electrosurgery is contraindicated in cases of extrinsic compression of the airway.

**Snares**

The use of a monopolar snare is especially suitable in cases of pedunculated tumors. After the snare has been placed around the tumor, the tumor can be severed from the base using coagulation current. The snare should not be closed too quickly during removal in order to prevent a purely mechanical resection with no coagulation. Bleedings can be controlled with the snare and a coagulation mode. This enables the majority of the tissue to be removed without damage, making it suitable for subsequent pathological examination.

**Needle knives**

Cutting modes such as the endoCUT®, which offers additional coagulation, are suitable for monopolar needle knives. Their use is described for web-like stenoses that circumferentially obstruct the airways. Needle knives can be used to perform incisions on these stenoses followed by dilation with a balloon. Care should be taken when using needle knives because they can cut through bronchial walls and cartilage. Here, endoCUT® mode enables a stepwise technique with activation using only one button and with coagulation current between each step. Amat et al. used the following endoCUT® I settings: Effect 1, Cutting duration 3, Cutting interval 3.

**Coagulation probe or monopolar forceps**

Airway obstructions, for example, can be ablated with coagulation probes or monopolar forceps. Following tissue contact, a soft coagulation current is applied with the coagulation probe or monopolar forceps. Tremblay et al. describe the advantages of the autostop function, which indicates that the coagulation was successful. Without autostop, the whitish discoloration of the tumor indicates successful devitalization. The lesion is treated from the base up and from proximal to distal. Then, the ablated tissue is removed, for example with a forceps or the rigid bronchoscope.

The coagulation instrument should be cleaned regularly during the application in order to maintain conductivity. When working with a coagulation probe, increased caution is recommended so as not to damage the airway wall and cartilage. Detailed knowledge of the anatomy of vascular structures surrounding the airway is also crucial to avoid complications.

**Clinical results**

The use of flexible coagulation instruments has been described in various publications as effective in patients with airway obstructions.

- Sutedja et al. describe successful recanalization using coagulation probes in 70% of cases
- Tremblay et al. summarize other results involving the use of the electrosurgical instruments described above for malignant airway obstructions. They found successful treatment of malignant airway obstructions in 53% to 100% of cases.
- Other authors report success rates of between 70% and 80%
BLEEDING MANAGEMENT

Electrosurgery enables bleeding to be quickly controlled in the case of hemorrhages in the lung. 35,38,36
Bleeding can be controlled by placing the coagulation instrument on the target tissue and activating the softCOAG® or forcedCOAG® mode for a few seconds.

SAFETY

Complications directly related to electrosurgery are rare. 35,36 They include tracheal fire at excessive oxygen concentrations above 40 % and airway perforations when electrosurgery is combined with radiation. Other complications include bleeding, pneumonia, myocardial infarction, stroke and hypoxia. 35,32,26 Tremblay et al. point out that the small number of studies makes it difficult to estimate the exact incidence rate of major complications. It is estimated that these complications occur in less than 5 % of cases when good patient selection practices and attention to detail during the procedures are maintained. 35 Folch et al. estimate the risk of significant bleeding at 2-5 %. 25

Comparison with laser therapy

The indications for the use of electrosurgery in the lung are identical to those for laser therapy and include palliative treatment of malignant as well as benign airway obstructions. 26,36,32,27 Here, the authors underscore less expensive electrosurgery. Tremblay et al. supplement this with further advantages, such as absence of laser specific safety precautions, lower risk of airway perforation and a steeper learning curve. 35 Although no randomized studies are available, multiple authors report comparable results with electrosurgery. 35,38 Bollinger et al. describe electrosurgical contact modes as comparable to Nd-YAG lasers and emphasize that the principle is straightforward and easy to comprehend and use. 36
Argon plasma coagulation

Argon plasma coagulation (APC) is applied in the lung to coagulate benign and malignant tissue changes, ablate tissue, and control bleeding. Argon plasma coagulation is an expanded application of monopolar electrosurgery. Ionized argon gas (plasma) is used to conduct electric current to the target tissue. APC thus provides a contact-free tissue coagulation and bleeding control. 39,36,27,26,35,38,32

**ARGON PLASMA COAGULATION TECHNIQUE**

As in monopolar electrosurgery, current (IHF) flows in a closed loop for APC application: from the unit to the instrument, then through the patient’s body to the return electrode (NE), and finally from the return electrode back to the unit. In argon plasma coagulation, electric current is conducted with no contact. The APC unit conducts the argon gas (Ar) via the flexible probe to the tip of the probe, where it exits and flows into the target area. The current (IHF) is transmitted via a metal wire that runs through the probe and transmits the current from the generator to the tip of the probe. The argon gas is ionized at a voltage of approx. 4000 V. A conductive plasma is formed that can transmit the electric current from the tip of the wire in the probe to the target tissue. This transmission takes place in the form of electric arcs with a range of up to 10 mm, depending on the setting. 39 These are transmitted to the site nearest the APC probe tip based on the principle of least resistance, regardless of whether the tissue is in front or to the side of the electrode and regardless of the flow direction of the argon gas. This enables lateral applications with APC. 26,40
Tissue effects of APC

As in the case of contact coagulation, argon plasma coagulation heats the target tissue with a monopolar flow of current. However, as a non-contact procedure, APC has a lower penetration depth than for example coagulation with softCOAG®, because the effect is self-limiting to a certain degree due to tissue drying (desiccation).32

FACTORS INFLUENCING THE TISSUE EFFECT

The following main factors have an influence on APC coagulation. They are listed in order of relevance:41

1. Application duration (especially for static application):
The self-limiting effect of APC is due to the drying (desiccation) of the tissue and resulting reduction in conductivity. However, deeper penetration depths are possible with a longer application duration. The following applies: The longer APC is applied, the deeper the effect on the target tissue. For this reason, we recommend starting with short activation times and increasing the duration step by step up until the desired tissue effect is achieved under visualization.

2. Power limitation/effect level:
The power limitation should be set on the HF generator depending on localization and size (diameter, depth, convexness) and the lesion to be treated. Low power limitation settings (e.g. 20 watts/effect 2) are suitable for superficial, small lesions. Medium power limitation settings (e.g. 30–40 watts/effect 3–4) are ideal for devitalizing or reducing tumors or to control bleeding. High power limitation settings (e.g. 50 watts/effect 5) are especially suitable for palliative tumor treatment, e.g. for ablation of larger exophytic tumors and for stenosis recanalization.

3. Probe distance to target tissue
The tissue effect decreases with increasing probe distance and ignition breaks down. It is important to ensure that the direction of coagulation is determined by the direction of the argon flow and the shortest distance between the nozzle and the tissue.39

4. Static and dynamic application
In the case of longer, static APC application, the depth effect increases greatly. If the application duration is too long, the tissue may be carbonized and perforated. We therefore recommend short activation times of 1 to 2 seconds with static application in superficial lesions. In dynamic application, the APC probe should be moved under visual control in slow, controlled movements (brushstrokes) over the target tissue.

5. APC mode
Different tissue effects are possible, depending on the APC mode setting (see below). They are characterized by different depth effects and varying coagulation and desiccation rates.

THERMAL EFFECT ZONES

Depending on different influencing factors, the following thermal effect zones arise and propagate radially into the depth:

1. Vaporization: Tissue vaporizes due to extreme heat
2. Carbonization: The tissue burns and turns black
3. Coagulation/Desiccation: The pronounced desiccation effect of APC causes tissue shrinkage that contributes to immediate tumor reduction
4. Devitalization: At higher temperatures, cell devitalization sets in with simultaneous hemostasis through denaturation of proteins
5. Hyperthermia: Depending on the duration of application, the tissue can recover or die (devitalization)
Differences in APC modes

The following generally applies: The energy transmission per unit of time with pulsedAPC® Effect 1 and 2 is comparable to that of forcedAPC with the same effect setting. This results in the same coagulation depth per unit of time with static application at one site and with the same effect setting.

However, different modulation and pulses with pulsedAPC® result in varying tissue effects that can be used in different ways with dynamic application. Thus, pulsedAPC® with Effect 1 supports a stepwise technique, while pulsedAPC® with Effect 2 and forcedAPC enable a continuous technique.

forcedAPC

This mode for argon plasma coagulation continuously transmits electrical energy to the target tissue. There, it produces effective coagulation with desiccation of the tissue. The depth effect is decreased by the rapid desiccation of the tissue.

pulsedAPC®

This APC mode transmits the electrical energy with a pulsing on/off activation of the argon beam. pulsedAPC® provides a slow (Effect 1) and fast (Effect 2) mode.

- pulsedAPC®, Effect 1: High energy transmission per pulse with longer pulse pauses
- pulsedAPC®, Effect 2: Higher pulse frequency with lower energy transmission per pulse

The average energy transmission per unit of time is identical for both modes.

Coagulation depth (y-axis in mm) vs. effect setting (x-axis) at an application time of 5 seconds
APC probes consist of a thin tube that is introduced via the working channel of a flexible bronchoscope. The tube contains a metal wire that conducts electric current to the tip of the probe, which is equipped with a resistant tungsten electrode. Upon activation, argon gas is released from the tip of the probe and forms the plasma under high voltage that generates the tissue effect. APC probes for interventional pulmonology by Erbe have a probe diameter of 1.5 mm or 2.3 mm and can be used in the central lung region under visualization. The probes are flexible and have axial, lateral (side fire) and radial (circumferential) beam forms (see below).

Axial probes are universally applicable and available in 1.5 mm and 2.3 mm. They enable applications in different situations, especially axial applications.

The side-fire variant is available in 2.3 mm and enables a precise application because the argon beam is only directed via a lateral opening.

The circumferential beam form is especially suitable for lateral applications. The ceramic head preserves the tissue in front of the probe during application.

The pulsedAPC® or forcedAPC modes described above can be selected for the various applications, such as hemostasis, devitalization or recanalization.
APC applications

BLEEDING MANAGEMENT

Since 1991, APC in flexible endoscopy has been increasingly used to control bleeding in the gastrointestinal tract.39 In addition to applications in the field of gastroenterology, APC in flexible bronchoscopy is used to control bleeding in the tracheobronchial tract.39,16,27,28,31,35,38,32 Some authors consider bleeding control as the best indication for flexible APC in the lung39, others consider it even as the method of choice.39

Technique

APC as a non-contact method can be used to control bleeding by using the plasma to coagulate the desired region. In order to control bleeding and in the case of other APC applications, it is important to note that the direction of coagulation is determined by the direction of the argon flow and the shortest distance between the nozzle and the tissue.39

Clinical results

The treatment of hemoptysis and control of bleeding with tumors are described as safe and effective.35,39,42 Reichle et al. describe successful bleeding control in 118 out of 119 patients with the flexible as well as the rigid technique.39 Morice et al. treated hemoptysis in a group of 56 patients with 100% successful bleeding control. One of the success factors for patient selection: Bleeding in the central lung region accessible with the bronchoscope.40

RECANALIZATION

Endobronchial malignant and benign tumors can be recanalized using flexible APC applications.

Other described applications include:

- Recanalization of occluded stents
- Treatment of fistula conditioning before fibrin adhesion
- Removal of granulation tissue
- Treatment of scarring stenoses

Technique

In addition to the properties of APC for tissue desiccation, recanalizations with APC are described in combination with mechanical extraction are described in the literature.39,40 Here, an APC penetration depth of up to 3 mm is used in order to initially ablate the tumors. The pronounced desiccation effect also causes tissue shrinkage that contributes to immediate tumor reduction. This reduction was up to 50% in bronchial tumors. The application time was 5 seconds.39

Reichle et al. describe the most applications with rigid intubation with jet ventilation and flexible bronchoscopy. Following successful ablation, the devitalized tissue is extracted using the rigid bronchoscope or a forceps.42 Once the devitalized tissue layer is extracted, the step is repeated. APC is also suitable to control bleeding during the application. Applications with flexible intubation are also described.39,40

Depending on the situation, it can be necessary to repeat the bronchoscopy 1-3 days later in order to extract necrotic tissue and fibrin plaques. Follow-up bronchoscopies at 3 months are described as well.39,40

Clinical results

The reviewed data revealed successful and complete recanalizations using the technique described above in 67% of cases with an additional 29%, in whom a minor reopening of the airways was possible.39 Other data reveal improved symptoms following recanalization in 98% (59/60) of cases.42
DEVITALIZATION AND OTHER APPLICATIONS

APC is suitable for ablation in a variety of disorders.36,45

Technique
Through ablation with APC, the target tissue is coagulated using the non-contact method.

Clinical results
The treatment of superficial squamous cell carcinomas with few cell layers is described. One of the advantages described is the ability to quickly devitalize large areas with low depth effect.36
The extraction of pleomorphic adenomas, the closure of a bronchoesophageal fistula, and applications with mucoepidermoid carcinomas are also described.45
Jin et al. 2013 describe the use of APC to treat tumorous endobronchial tuberculosis. The success rate was better in the argon plasma coagulation/chemotherapy group than in the chemotherapy-only group. The authors conclude that APC can accelerate the healing of tumorous endobronchial tuberculosis and can help prevent progressive bronchial stenosis resulting from tumorous endobronchial tuberculosis. Described complications include laryngeal spasm, cough, and minor bleeding.46

Safety
APC is considered safe for recanalization.39,40,45 Described complications vary between no complications40 to perforations with pneumomediastinum and subcutaneous emphysema, pneumothorax, endobronchial fires (with no injury), and wall necrosis.39
Reichle et al. point out that the success of the intervention did not depend on the APC technique, but rather on the proper establishment of a clear indication. The summary of all complications resulted in a rate of 3.7 %. Reichle et al. report that two patients (0.4 %) died within 24 hours, but that these deaths were not directly attributable to APC.

Gas embolisms cannot be completely ruled out, which is why Reichle et al. recommend the following additional precautions:

- Minimize the argon gas flow to < 1.5 l/min.
- Activate the APC for up to 5 seconds max.
- Control or limit the endoluminal pressure (ventilation pressure).
- Restrict application to vessels with a diameter of < 3 mm.
- Discontinue the supply of enriched oxygen during activation of APC in the vicinity of flammable materials (e.g. plastic stents).

Other recommendations include switching off39 or reducing the oxygen supply to ≤ 40 % during application of a monopolar technique in the lung.32,37,39,40

COMPARISON WITH ELECTROSURGICAL CONTACT COAGULATION

In comparison with electrosurgery, a lower risk of bleeding and a time savings during devitalization of larger areas was found for APC as compared to monopolar contact coagulation.40
The lateral and retrograde application options of APC are also considered advantageous in comparison with the contact method.26

COMPARISON WITH LASER

Laser is a standard procedure for tumor extraction. Endobronchial laser therapy success rates of 75-92 % have been reported for recanalizations. As a result, therapeutic outcomes with laser and APC are comparable. Disadvantages described for laser include high costs, fixed location, safety precautions, limited hemostatic effect, and perforation risk.19 This perforation risk is lower with APC because the tissue effect is self-limiting and more superficial with increasing resistance.20 Application advantages, such as better hemostasis properties39 or lateral and retrograde application options are underscored.19,36,18,40 Ernst et al. mention these application advantages as particularly relevant to the upper lobes and apical segments of the lower lobes of the lung.18
Information on safe use of APC and electrosurgery

RETURN ELECTRODE

Use of a return electrode is associated with a risk of burns due to incomplete contact between the electrode and the patient or incorrect positioning.

When connected to a split return electrode, modern electrosurgical units (e.g. VIO® 3) can determine whether the return electrode is positioned correctly. The Erbe NESSY® safety system checks the electrode for correct placement by constantly comparing the current from both return electrode surfaces. In the case of major differences, activation is interrupted with a warning signal. In addition, some return electrodes are equipped with an equipotential ring (e.g. NESSY®Ω) that evenly distributes the electrical energy to the return electrode. We recommend using NESSY®Ω to maximize safety in monopolar electrosurgery.

OXYGEN CONCENTRATION

One potential complication of the monopolar technique are fires in the lung that can result from the administration of additional oxygen. As a result, it is recommended to switch off the oxygen supply when using monopolar technologies or reduce it to ≤ 40% during application.

ACTIVE IMPLANTS

Monopolar electrosurgery can adversely affect pacemakers and other active implants sensitive to electrical energy. We recommend consulting the respective department of the hospital. In addition, the return electrode must be attached such that the current is not conducted over the implant.

ARGON GAS FLOW

The maximum argon gas flow in the lung is discussed by different authors in the literature. Due to the potential complication of gas embolisms, we recommend maintaining the argon flow as low as possible.

The default values for the Erbe APC probes are as follows:

<table>
<thead>
<tr>
<th>PROBE TYPE</th>
<th>ARGON FLOW DEFAULT SETTING</th>
</tr>
</thead>
<tbody>
<tr>
<td>FLEXIBLE PROBE, 1.5 MM IN DIAMETER</td>
<td>0.3 L/Min</td>
</tr>
<tr>
<td>FLEXIBLE PROBE, 2.3 MM IN DIAMETER</td>
<td>0.8 L/Min</td>
</tr>
<tr>
<td>FLEXIBLE PROBE, 2.3 MM IN DIAMETER, SIDE-FIRE</td>
<td>0.6 L/Min</td>
</tr>
<tr>
<td>FLEXIBLE PROBE, 2.3 MM IN DIAMETER, CIRCUMFERENTIAL</td>
<td>0.8 L/Min</td>
</tr>
</tbody>
</table>

DISTANCE OF INSTRUMENTS TO BRONCHOSCOPE TIP

Thermal damage to the bronchoscope may result due to the effect of monopolar current on the bronchoscope tip under certain conditions. As a result, it is recommended to only activate the probes when they are protruding by at least one centimeter (black mark on Erbe probes) from the bronchoscope.
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Important information

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