

Catheter Access Port (Computed Tomography) Myelography in Intrathecal Drug Delivery Troubleshooting: A Case Series of 70 Procedures

Elmar M. Delhaas, MD*[†] ; Biswadjiet S. Harhangi, MD, PhD, MSc[‡] ;
Sander P.G. Frankema, MD, PhD*; Frank J.P.M. Huygen, MD, PhD*;
Aad van der Lugt, MD, PhD[†]

Objectives: Intrathecal drug delivery is used for the treatment of intractable spasticity, dystonia, and pain. When the symptomatology fails to respond to therapy, the cause could be failure of the medication infusion. The purpose of this study is to assess pump catheter access port (CAP)-myelography and CAP-CT-myelography as advanced imaging methods in treatment failure.

Materials and Methods: We analyzed observational routinely collected data of 70 CAP procedures with 2D/3D reconstructions and additional imaging of 53 adult patients where the cause of treatment was unclear between November 2013 and November 2018. CAP-myelography and CAP-CT myelography were performed with postprocessing 2D/3D reconstructions. When myelography could not be obtained or when the result did not reveal the cause of the treatment failure, additional procedures, such as noncontrast CT, MRI, lumbar puncture CT, and 111Indium-DTPA SPECT-CT, were performed.

Results: CAP fluid aspiration prior to contrast medium injection was not possible ($N = 17$). In one case, contrast was injected into the pump pocket unintentionally ($N = 1$). Of 70 procedures, 24% were unaspirable. The remaining CAP myelography examinations ($N = 52$) had limited value for the diagnosis. CAP-CT myelography ($N = 50$) was normal ($N = 31$). The abnormal results ($N = 19$) were dorsal dural leak ($N = 5$), subdural catheter position ($N = 2$), limited rostral flow of contrast material ($N = 4$), limited and abnormal contrast distribution ($N = 3$), obstruction of rostral flow ($N = 2$), a leak at the pump-catheter connection ($N = 1$), and a sheared catheter localized in the pump pocket ($N = 2$). Limited contrast distributions were found to be false positive findings ($N = 2$). Four normal CT-CAP myelographic procedures were false negatives, as the reference tests revealed a cause of intrathecal drug delivery (ITDD) failure. The CAP-CT procedures resulted in a sensitivity of 81% (17/21) and a specificity of 93% (27/29).

Conclusions: CAP-CT myelography with 2D/3D reconstructions is an essential step in the diagnostic algorithm for cases involving ITDD failure.

Keywords: Catheter access port, computed tomography, intrathecal therapy failure, myelography, programmable pump

Conflict of Interest: Dr. Delhaas reports personal fees from Medtronic, as a previous consultant, outside the submitted work; Prof. Huygen reports grants and personal fees from Abbott, personal fees from Grunenthal, outside the submitted work. In addition, Dr. Huygen has a patent 2,022,004 in the Netherlands pending. Prof. van der Lugt reports grants from GE Healthcare, Siemens, Stryker, Medtronic and Penumbra outside the submitted work. Dr. Harhangi and Dr. Frankema have nothing to disclose.

Address correspondence to: Elmar M. Delhaas, MD, P.O. Box 2040, 3000 CA Rotterdam, The Netherlands and Dr. Molewaterplein 40, Building Na-17, NL-3015 GB Rotterdam, The Netherlands. E-mail: e.delhaas@erasmusmc.nl

* Center for Pain Medicine, Erasmus MC University Medical Center Rotterdam, Rotterdam, The Netherlands;

[†] Department of Radiology and Nuclear Medicine, Erasmus MC University Medical Center Rotterdam, Rotterdam, The Netherlands; and

[‡] Department of Neurosurgery, Erasmus MC University Medical Center Rotterdam, Rotterdam, The Netherlands

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INTRODUCTION

Several observational studies demonstrate the value of intrathecal drug delivery (ITDD) for therapy-resistant spasticity, dystonia, and pain (1–3). Older data show a high complication rate, mainly related to the intrathecal catheter, with this rate varying widely among treating specialists (4–7). Current complications are related to the handling of the delivery system itself, as well as to its implantation or the underlying condition of the patient. As result of catheter improvements, the complication rate seems to have been considerably reduced (8,9).

Based on referred patients, we conclude that, in ITDD failures, advanced imaging procedures are frequently not performed or performed inadequately, which can lead to undertreatment, unnecessary surgery, or even unjustified termination of therapy. Algorithms for troubleshooting and the involved diagnostic procedures are subject to debate. One topic in this discussion is the role of catheter access port (CAP) computed tomography (CT) myelography as an advanced diagnostic procedure. Saulino et al (10) stated that the CAP-CT procedure should be part of the standard approach. However, it was recently suggested that the use of this procedure should be limited to emergencies and that it should not be considered as a routine examination (11). The aspiration failure rate of the CAP puncture, the nonphysiological flow of contrast material in the intrathecal space, the probable lower costs, and the lower radiation dose of ^{111}In -diethylenetriamine-penta-acetic acid scintigraphy (^{111}In -DTPA) single-photon emission CT (SPECT-CT) were presented as arguments (11).

Application of additional SPECT-CT imaging to the planar scintigraphic images led to improvement, but clinical experience is limited (12–14), and the interpretation of leakage thus does not seem to be precise (15). Nevertheless, SPECT-CT, which allows for the anatomical localization of a disorder, is essential when scintigraphy is applied. However, low-dose energy SPECT-CT will lead to a lower quality of imaging in comparison with CAP-CT myelography. In our opinion, ^{111}In -DTPA SPECT-CT and CAP-CT myelography are not entirely comparable. Both have a place in the ITDD troubleshooting algorithm, and the choice of procedure seems to be more a matter of preference concerning the sequence in the algorithm. The dynamic character of scintigraphy offers the unique possibility of following the tracer distribution over a time frame of several days and determining the location of the problem but has the issue that ^{111}In -DTPA radioactive substance is unavailable in an emergency. CAP-CT myelography with more high-resolution imaging could be crucial in determining the location and magnitude of the disorder. Although both procedures have been performed for several decades, published data are scant and it is unclear how many patients have undergone ^{111}In -DTPA SPECT-CT or, to the best of our knowledge, even absent for CAP-CT myelography. The consequence is a lack of a consensus regarding the optimal procedures and diagnostic criteria for determining ITDD failure (16). A comparison of the two methods could only be made with the same patients and after extensive evaluation and is therefore beyond the scope of this report.

The CAP procedure is not always easy to perform, which could be one of the reasons for its omission from the standard diagnostic approach. Technical skills, the position of the implanted pump, the possible presence of severe fibrotic reaction around the pump, and the vulnerable needle for CAP puncture are relevant factors. In ITDD failures, advanced imaging procedures are frequently not

performed or are performed inadequately, which can lead to undertreatment, unnecessary surgery, or even unjustified termination of therapy. Over the last few years, we have routinely used CAP myelography and fluoroscopy, combined with CT and 2D multiplanar reformation (MPR) (17), 2D maximum intensity projection (MIP) (17), and 3D volume-rendering technique (VRT) (17) reconstructions, in troubleshooting. The intended use of the CAP-CT procedure was to diagnose catheter leaks or obstruction or abnormal rostral distribution of the injected contrast material. The motivation for this retrospective observational study focused on routinely collected data was the paucity of information concerning the performance and the results of CAP (CT) myelography. Therefore, we aimed to assess the value of and the various factors involved in maximizing the diagnostic use of CAP (CT) myelography as an advanced imaging method in ITDD troubleshooting. The primary approach was the analysis of the application of CAP (CT) myelography in ITDD troubleshooting. When the procedure did not reveal the diagnosis, we performed additional steps to reach a definite conclusion.

MATERIALS AND METHODS

Patients

We included all routinely collected data from 70 CAP (CT) myelography procedures in 53 adult patients who were evaluated for ITDD failure between November 2013 and November 2018. Fifty-two of the patients were referred to our hospital for ITDD troubleshooting, when the referring neuromodulation center could not solve the problem of ITDD treatment failure. Our diagnostic procedures were prompted by the suspicion that the therapy was suboptimal or absent in its effect, leading us to question the efficacy of drug delivery. In all patients, a SynchroMed II pump model 8637 was implanted in the abdominal region together with the associated intrathecal catheters (Type 8731SC or Ascenda 8780/8781) (Medtronic Inc., Minneapolis, MN, USA). The lack of precise information concerning the pump and catheter application of the referred patients did not allow investigation of the incidence of their complication rate in a time frame. CAP-(CT) myelography was considered in treatment failure with severe symptomatology (18). In mild cases, the procedure was performed when the failure could not be managed with dose adaptations by a bolus administered by the pump or a lumbar puncture (18) in combination with conservative nonpharmaceutical treatment. Furthermore, a requirement was that the cause was not identified as being related to the patient's history, a signaled pump failure or a programming error in the pump readout, an unexpectedly empty pump, or abnormal plain radiography. ITDD failure was defined as the presence of one or more of the following criteria: a decrease in effectiveness of treatment, discrepancies between accurate aspirated volume versus interrogated reservoir volume, manifest- or occult-drug cerebrospinal fluid (CSF) leakage, repeated dosage increases without clinical improvement, and dosages exceeding 50% of the maximum recommended dosage with an insufficient clinical result (19,20). The first and last authors reexamined the images, taking all clinical features into consideration. Their assessments were focused on the distribution of the contrast medium injected via the CAP, the pump shape, catheter-pump connections, the course of the catheter, the catheter-catheter connection, the dural insertion, and the intrathecal distribution. When CAP

(CT) myelography did not reveal the diagnosis or when there was doubt concerning it, we carried out additional imaging procedures and discussed their results. The majority of other procedures involved ^{111}In -DTPA SPECT-CT scintigraphy. The study was approved by the medical ethics committee of our center (MEC-2017-326); in addition, given that this study is based on routinely collected procedure data that were retrospectively analyzed, meaning that the study had no impact on the patient, the requirement to obtain informed consent was waived.

CAP Myelography

CAP insertion using a 24-G non-coring Huber needle was performed under fluoroscopy under strictly sterile conditions. We found that, with the template provided with the CAP kit (Model 8540; Medtronic Inc.), the CAP funnel position could not be recognized in all cases. During fluoroscopy, we use a metal object (e.g., a surgical clamp or a pair of tweezers) to determine the CAP funnel's location. We positioned the C-arm fluoroscopy device such that the beam was parallel to the CAP axis, which allowed perpendicular needle insertion into the funnel. To prevent an injection overdose caused by the flushing of the highly concentrated catheter content into the intrathecal space, we first aspirated 2 mL of fluid (21). When we could not aspirate, we omitted the contrast material injection and terminated the procedure or when not performed previously, a noncontrast CT scan. After successful fluid aspiration, we injected 10 mL of contrast material (iohexol, Omnipaque 300, GE Healthcare B.V., Eindhoven, The Netherlands). Due to the high viscosity of the contrast material and the small needle diameter, we had to apply significant force during the injection. To reduce the force required, the contrast material was injected at body temperature. To ensure an optimal distribution of the contrast material in the CSF, we turned the patient to the left and to the right and placed him or her in the Trendelenburg position. Under fluoroscopy, we controlled the catheter pathway for leakages and the accurate intrathecal distribution of the contrast material. Thereafter, we performed a myelogram. Next, we flushed the catheter with 2 mL preservative-free saline fluid to remove the contrast material from the catheter. To prevent a withdrawal syndrome, we programmed the pump for a catheter-priming bolus injection, which was calculated based on the catheter length and drug concentration.

CAP-CT Myelography

Following CAP myelography, we performed a CT scan. The first, and largest, group of patients was evaluated using a single-energy CT (SECT) scanner. Prior to the CAP procedure, we implemented low-dose single-energy CT with postprocessing 2D/3D reconstructions with a low radiation exposure as a replacement for postoperative and noncontrast troubleshooting procedures, as recently suggested (22). This technique allows visualization of the entire drug delivery pathway. Catheter-related problems such as disconnection, dislocation, kinking, or twisting can be identified. However, for CAP-CT myelography, we need more precise information and used standard high-dose CT. We have recently switched from single-energy CT to dual-energy CT when applying this CT procedure (23). Therefore, we used the twin-beam dual-energy CT scan (Siemens Healthcare GmbH, Erlangen, Germany) with gold (Au) and tin (Sn) filters in combination in front of the 120 kVp X-ray beam (24). The filters split the beam into high- and low-energy X-ray spectra before it reaches the patient. Further image

improvement could be achieved with a metal artifact reduction algorithm (iMAR). The different x-rays provide dual-energy CT a further advantage over single-energy CT by providing more information when metal implants (e.g., the pump, catheter-catheter connector, or osteosynthesis material) are present in the scanned area. With this approach, the scattering caused by the metal parts could be reduced. Furthermore, leaks at the catheter-catheter and the pump-catheter connection could be distinguished from beam-hardening artifacts. Originally, we limited the reconstructed scan field of view to the spine. To obtain information concerning the entire implanted drug delivery system from the dorsal to the abdominal pump-implanted area, we extended the field of view to the extra-vertebral abdominal region. For the imaging of the intrathecal catheter and the distribution of the contrast material above the catheter tip, we applied a lumbar-cervical spine scan range. A breath-holding command was given to avoid pump movement during breathing. The scan parameters for dual-energy CT included the following: collimation: 300×0.6 mm; rotation time: 0.5 sec; and slice thickness: 0.8 mm. Although radiation exposure is crucial in CAP-CT myelography, the use of dual-energy with a higher radiation load instead of the original single-energy CT does not outweigh the importance of precise imaging. To further improve CAP-CT myelography imaging, we postprocessed the data on a workstation to 12-mm maximum intensity projections (17), which enables the imaging of highly intensive structures with respect to the surrounding structures, and to 1.5 mm multiplanar reformations (17), whereby thin-slice axial data were converted into coronal, sagittal, oblique, or curved planes, which allows one to follow the course of the implanted catheter. Using the volume-rendering technique (17), we transformed the axial data into 3D images.

Additional Imaging Procedures

In this study, when we could not aspirate CSF via the CAP and CAP(-CT) myelography was consequently not permitted, we still fulfilled the scheduled CT as a standard noncontrast CT to identify an epidural catheter. When the epidural catheter position was not clear, we additionally carried out lumbar puncture (LP) CT myelography. Our next diagnostic step when CSF could not be aspirated was ^{111}In -DTPA scintigraphy. To determine the anatomical position and to obtain detailed information concerning the identified abnormality, we combined the planar scintigraphy with SPECT-CT. To be certain of a normal rostral intrathecal activity distribution over time, we optimized the scintigraphy by standardizing the pump flow rate, as result of which the tip of the intrathecal catheter would typically be reached after 24 hours. Magnetic resonance imaging (MRI) was used to identify localized intrathecal abnormalities.

Statistical Analysis

The sensitivity and specificity of the different procedures were calculated by comparing the imaging assessment outcome as the index test, with the outcome of the gold standard reference test, which was based on all performed imaging procedures and clinical and surgical information. A true-positive result was thereby defined as when an abnormality could be demonstrated with the index test and the reference indeed revealed a cause of ITDD failure, a true negative when no abnormality was found with the index test and the reference test, a false positive when an estimated abnormality could not be confirmed by the reference, and a false negative when the abnormality was overlooked. Due to the limited number of noncontrast CT scan procedures, we omitted the calculations of accuracy.

RESULTS

CAP Procedures

Table S1 summarizes the patient characteristics, the results, and the standard references used, which were distilled from the results. We performed 70 procedures on 53 patients. No adverse

events were reported as a result of the procedures. In 13 patients, the method was conducted several times, which resulted in a total of 17 additional procedures. The reasons for these additional procedures were as follows: one patient's spasticity was under insufficient control and was exacerbated after two years ($N = 2$),

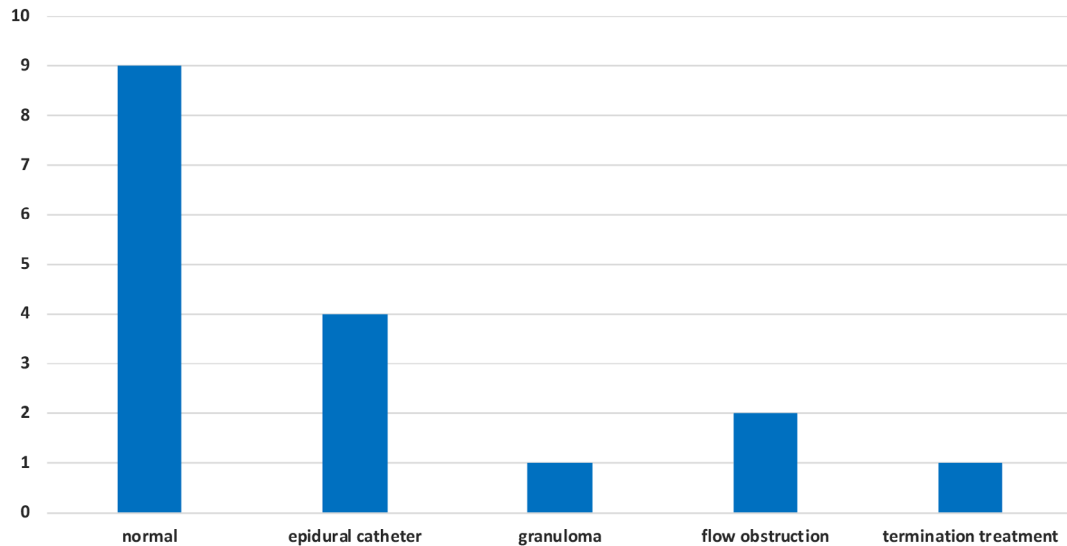


Figure 1. Results when via CAP cerebrospinal fluid could not be aspirated. [Color figure can be viewed at wileyonlinelibrary.com]

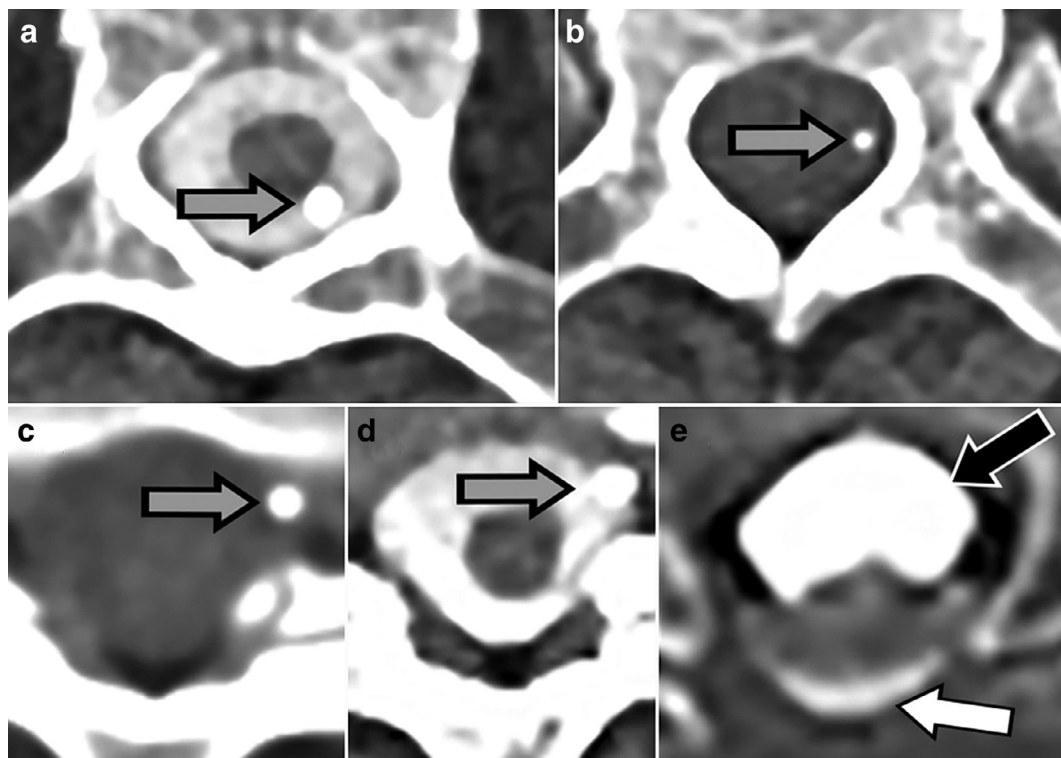


Figure 2. Catheter access port CT multiplanar reformation myelography revealed a normal intrathecal 8731SC catheter tip position (a, gray arrow) and a regular small-diameter Ascenda catheter tip position (b, gray arrow). The noncontrast CT multiplanar reformation image fostered suspicion of an epidural tip position of the 8731SC catheter (c, gray arrow). LP CT myelography confirmed the epidural position (d, gray arrow). CAP-CT multiplanar reformation myelography showed extensive subdural (e, black arrow) and minimal intrathecal (e, white arrow) contrast material, which explained the irregular contrast material distribution found with CAP myelography (Fig. 5c).

a persistent leak ($N = 2$), an unexplained reoccurrence of treatment failure ($N = 2$), a persistent treatment failure ($N = 8$), a limited effect after the surgical intervention ($N = 1$), to control a surgical intervention ($N = 1$), and when a broken catheter was replaced ($N = 1$).

CAP CSF Aspiration

In 17 procedures, we could not aspirate the CSF (Fig. 1), and contrast material was therefore not injected via the CAP. In nine of the 17 patients (53%) in which CSF aspiration was not possible, revealed a functional catheter based on scintigraphy with normal tracer distribution ($N = 5$), MRI with no abnormalities ($N = 2$), and a successful dose adaption ($N = 2$). Noncontrast CT scans showed an epidural catheter position ($N = 4$, Fig. 2c), which was confirmed by LP-CT myelography ($N = 1$, Fig. 2d), a downwards curved intrathecal catheter ($N = 1$), and normal findings ($N = 3$). ^{111}In -DTPA SPECT-CT demonstrated CSF flow obstruction ($N = 2$). Of the patients who refused further diagnostic procedures, one was

suspected to have catheter obstruction but wished to terminate the therapy.

CAP Myelography

In 53 procedures, we injected the contrast material via a needle positioned in the CAP (Fig. 3). Myelography could not be performed due to an unintended injection into the pump pocket ($N = 1$, Fig. 4a). Of the remaining 52 CAP-myelographies, 36 were normal. Sixteen revealed a suspected pump-catheter-related cause of ITDD failure, including catheter leak ($N = 2$, Fig. 5a), a downward curved catheter with possible reduced flow ($N = 1$), limited abnormal contrast distribution ($N = 6$, Figs. 5b,c), an acute stop in the contrast distribution ($N = 2$, Fig. 3d), and a limited normal-shaped contrast distribution ($N = 5$, Fig. 5e). In 12 of these 16 CAP myelographic procedures, the reference tests revealed a cause of ITDD failure, while, in four procedures, the limited contrast distribution ($N = 3$) and a downward curved catheter with possible reduced flow ($N = 1$) were found to be false positive findings. Eleven normal CAP myelographic procedures were false

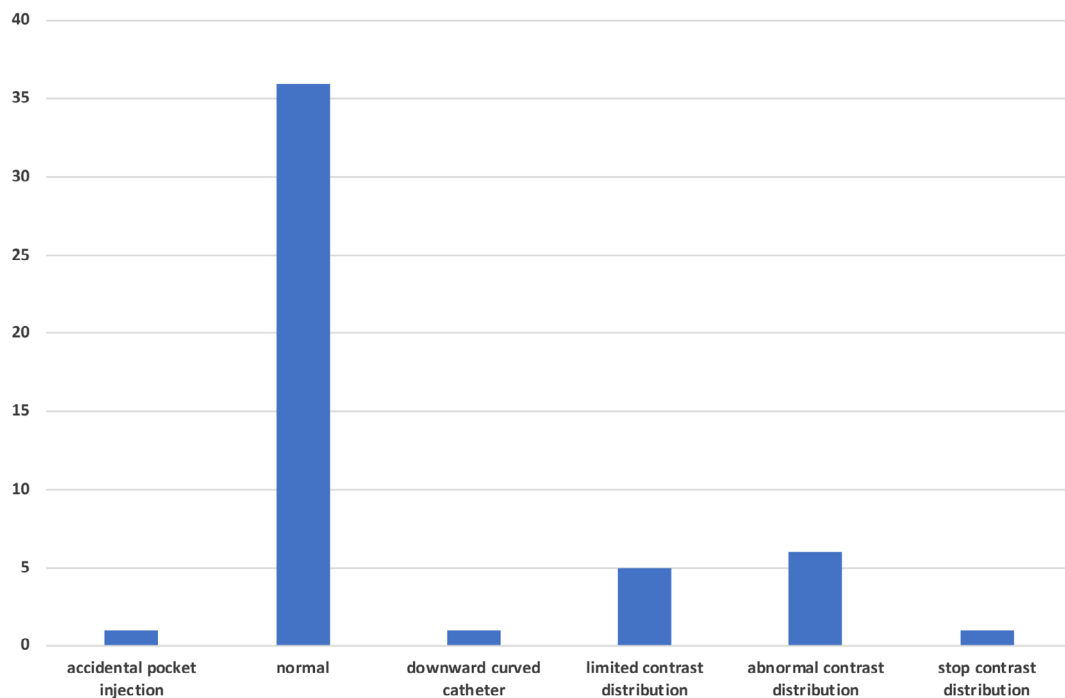


Figure 3. Results of catheter access port myelography. [Color figure can be viewed at wileyonlinelibrary.com]

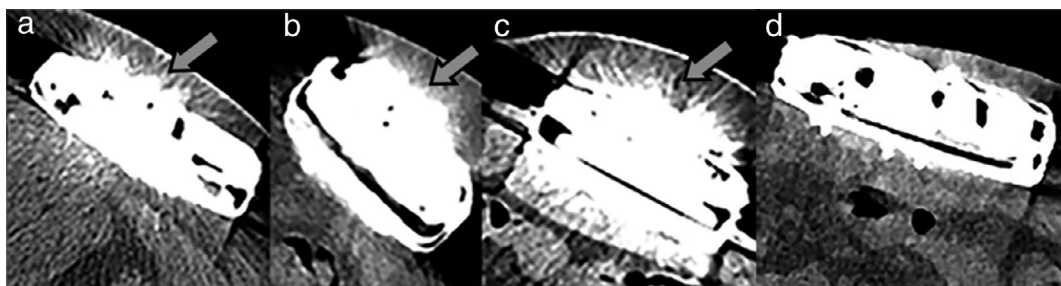


Figure 4. Scattering on catheter access port CT multiplanar reformation (gray arrow) images caused by contrast material in the pump pocket. At the procedure, 7 mL of contrast material was unintentionally injected into the pump pocket (a). A sheared catheter located in the pump pocket caused contrast material accumulation (b). Severe CSF and contrast material appearance in the pump pocket (c) as a result of a dorsal dural leak at the previous catheter insertion, where CSF passed retrograde along the implanted catheter, and a normal pump appearance after aspiration of the fluid and dural leak treatment with an epidural blood patch (d).

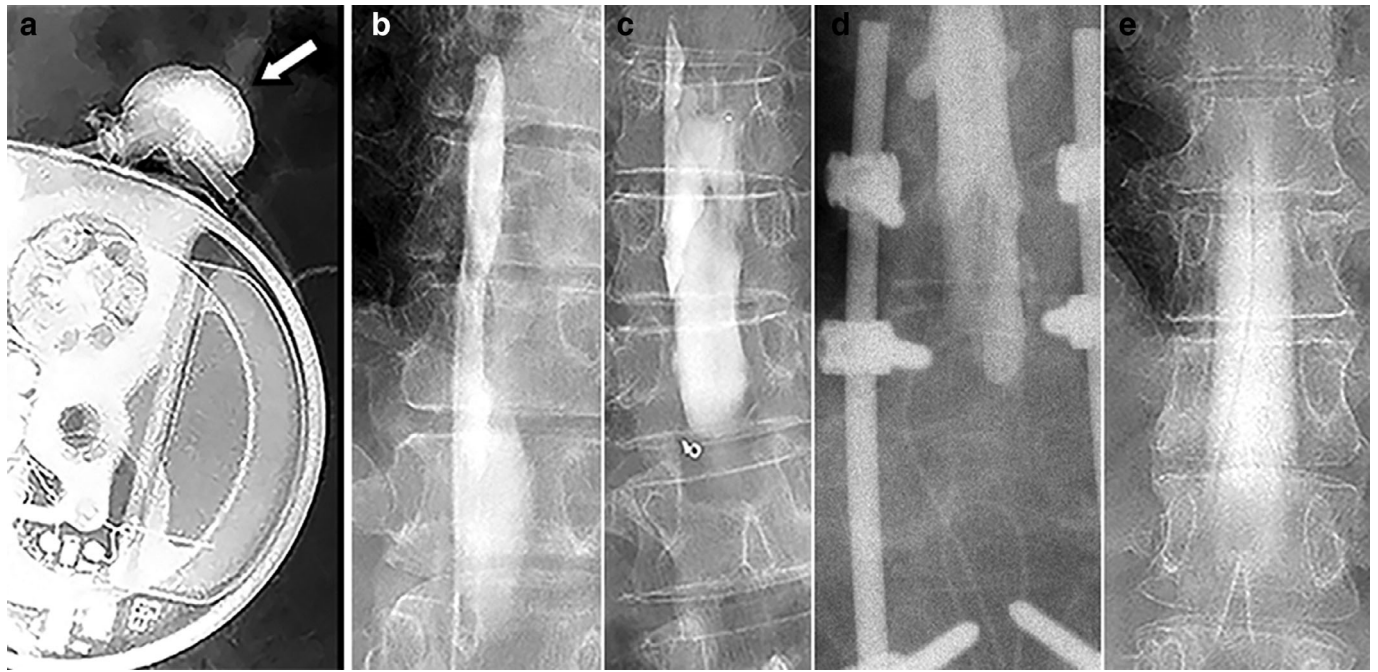


Figure 5. Catheter access port myelography revealed a pump-catheter connector leak (a, arrow), irregular distribution of the contrast material, caused by an intradural cyst (b), subdural catheter position (c), CSF flow obstruction (catheter tip position above the obstruction) (d), and an inadequate Trendelenburg maneuver (e).

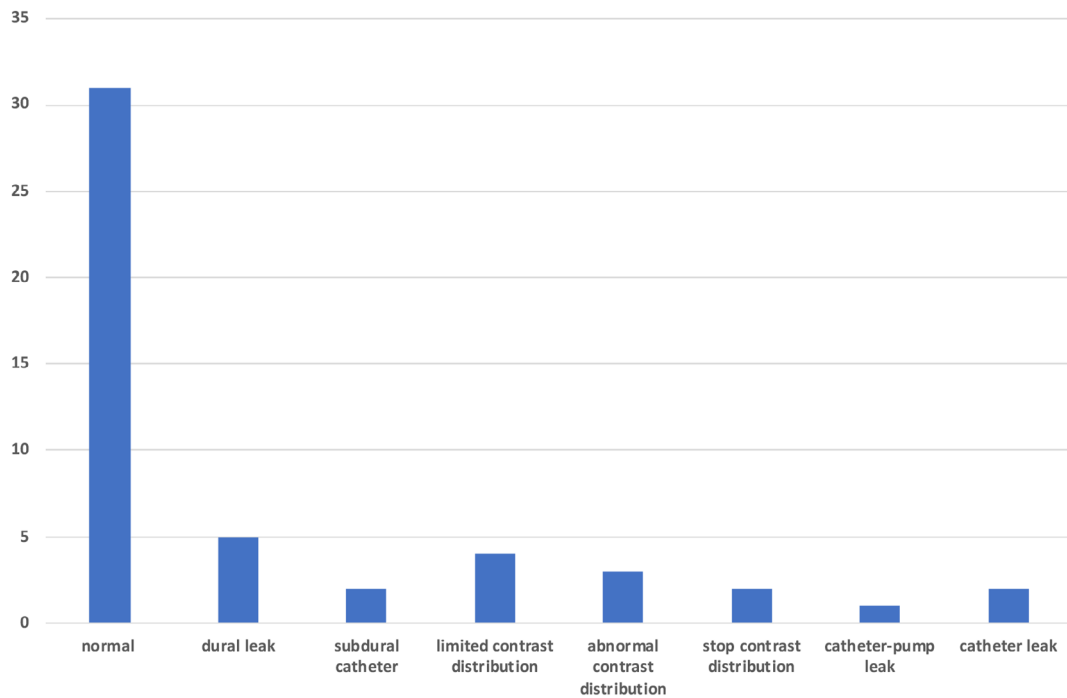


Figure 6. Results of catheter access port computed tomography myelography. [Color figure can be viewed at wileyonlinelibrary.com]

negatives, as the reference tests revealed a cause of ITDD failure. The calculated sensitivity of CAP myelography was 52% (12/23), with a specificity of 86% (25/29).

CAP-CT Myelography

We carried out 50 CAP-CT myelography procedures in which images of the spinal column were reconstructed (Fig. 6). In 24 of

these procedures, the field of view of the image reconstruction was enlarged to the extra-vertebral region, including the abdominal pump position and the extra-spinal catheter tract. CAP-CT myelography was diagnosed as normal ($N = 31$). Four of these normal CAP-CT myelographic procedures were false negatives, as the reference tests revealed a cause of ITDD failure. The findings included only spinal region evaluation ($N = 1$), while the catheter leak was present in the extra-vertebral region. Scintigraphy ($N = 3$)

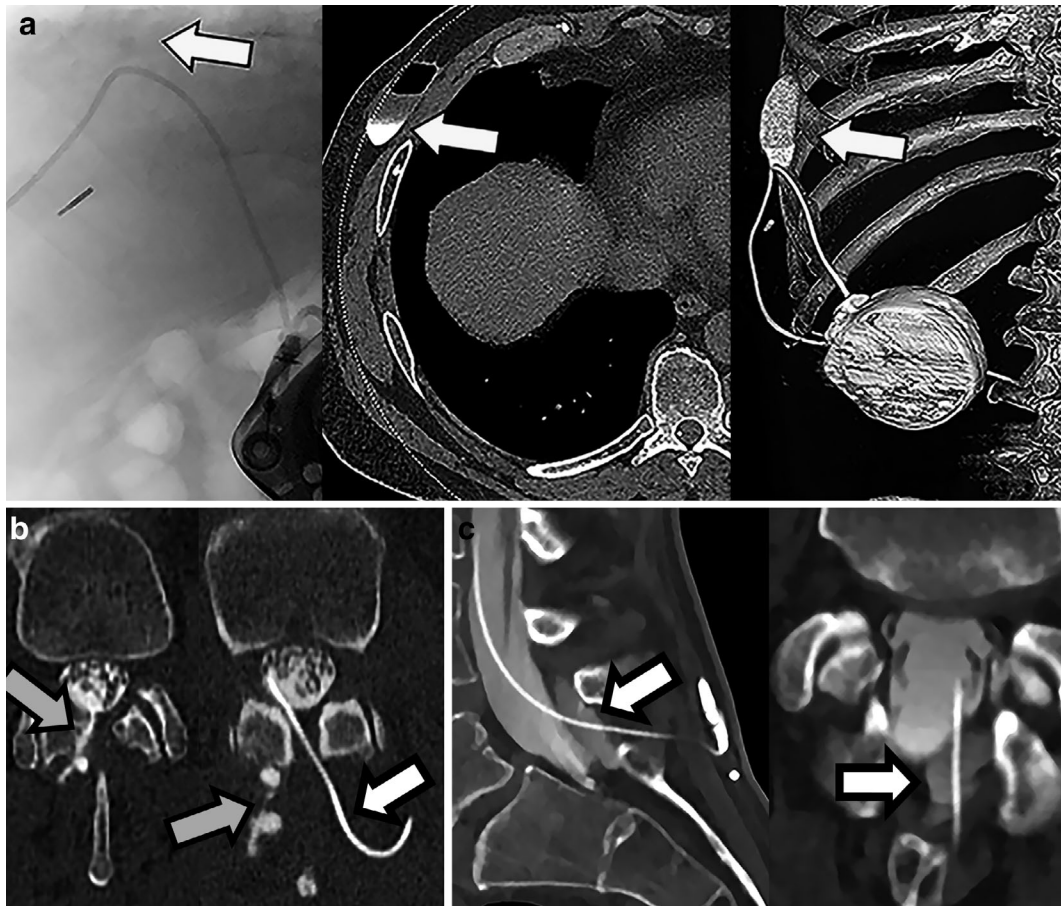


Figure 7. a, The tiny catheter leak was not recognized with catheter access port (CAP) fluoroscopic myelography (left, white arrow). CAP-CT multiplanar reformation myelography revealed abnormal subcutaneous contrast material accumulation (middle, white arrow). The 3D volume-rendering technique reconstructions demonstrated minor catheter leak (right, white arrow). b, CAP-CT multiplanar reformation myelography showed dural leak at the original insertion of a migrated catheter (gray arrow), with at the opposite site the newly inserted catheter (white arrow). c, CAP maximum intensity projection myelography showed minor extradural contrast accumulation, which was caused by a small dural leak (white arrow).

revealed a normal result ($N = 1$), whereby an intrathecal leak was found during surgical intervention, a catheter obstruction ($N = 1$), and a retrograde tracer distribution via a retained catheter ($N = 1$).

Spinal CAP-CT myelography revealed 16 suspected causes of ITB failure, including dorsal dural leak ($N = 5$, Fig. 7f,g), subdural catheter position ($N = 2$, Fig. 2e), limited rostral flow of contrast material ($N = 4$), limited and abnormal contrast distribution ($N = 3$), and obstruction of rostral flow ($N = 2$). The extra-vertebral image reconstructions revealed three causes of ITDD failure, namely contrast media around the pump owing to a leak at the pump-catheter connection ($N = 1$), a sheared catheter in the pump pocket ($N = 1$, Fig. 4b), and contrast material in the abdominal soft tissue due to a catheter leak ($N = 1$, Fig. 7b,c), the latter of which was not identified by CAP myelography (Fig. 7a). Dural leaks ($N = 5$) were defined as a loss of CSF from the intrathecal space. The loss could be postoperative or chronic and with or without clinical symptomatology. The observed leaks were caused by a previous catheter insertion site ($N = 4$, Figs. 4c and 7d,e) and occurred after the reinsertion of a catheter ($N = 1$, Fig. 7f,g). In two cases, the dural leak that was visible on the spinal CAP-CT myelography was accompanied by retrograde flow to the pump pocket, which was visible on the extra-vertebral image reconstruction (Fig. 4c). We could treat the dural CSF leaks with one to three

homolog epidural blood patches. In our approach, we injected slowly over a few minutes to a maximum of 20 mL or terminated the procedure when the patient complained of a headache.

In two procedures, a limited contrast distribution was found, which transpired to be false positive findings. CAP-CT myelography was normal in 31 procedures. Four normal CT-CAP myelographic procedures were found to be false negatives, as the reference tests revealed a cause of ITDD failure, including one examination in which only the spinal region was evaluated while a catheter leak was present in the extra-spinal region, one examination in which the follow-up scintigraphy was normal, but an intrathecal catheter leak was found during surgical intervention, one examination in which scintigraphy revealed catheter obstruction, and one examination in which scintigraphy revealed retrograde tracer distribution via a retained catheter. The CAP-CT procedures resulted in a sensitivity of 81% (17/21) and a specificity of 93% (27/29).

DISCUSSION

Based on the analysis of the observational retrospectively collected CAP and CAP-CT myelography data for troubleshooting

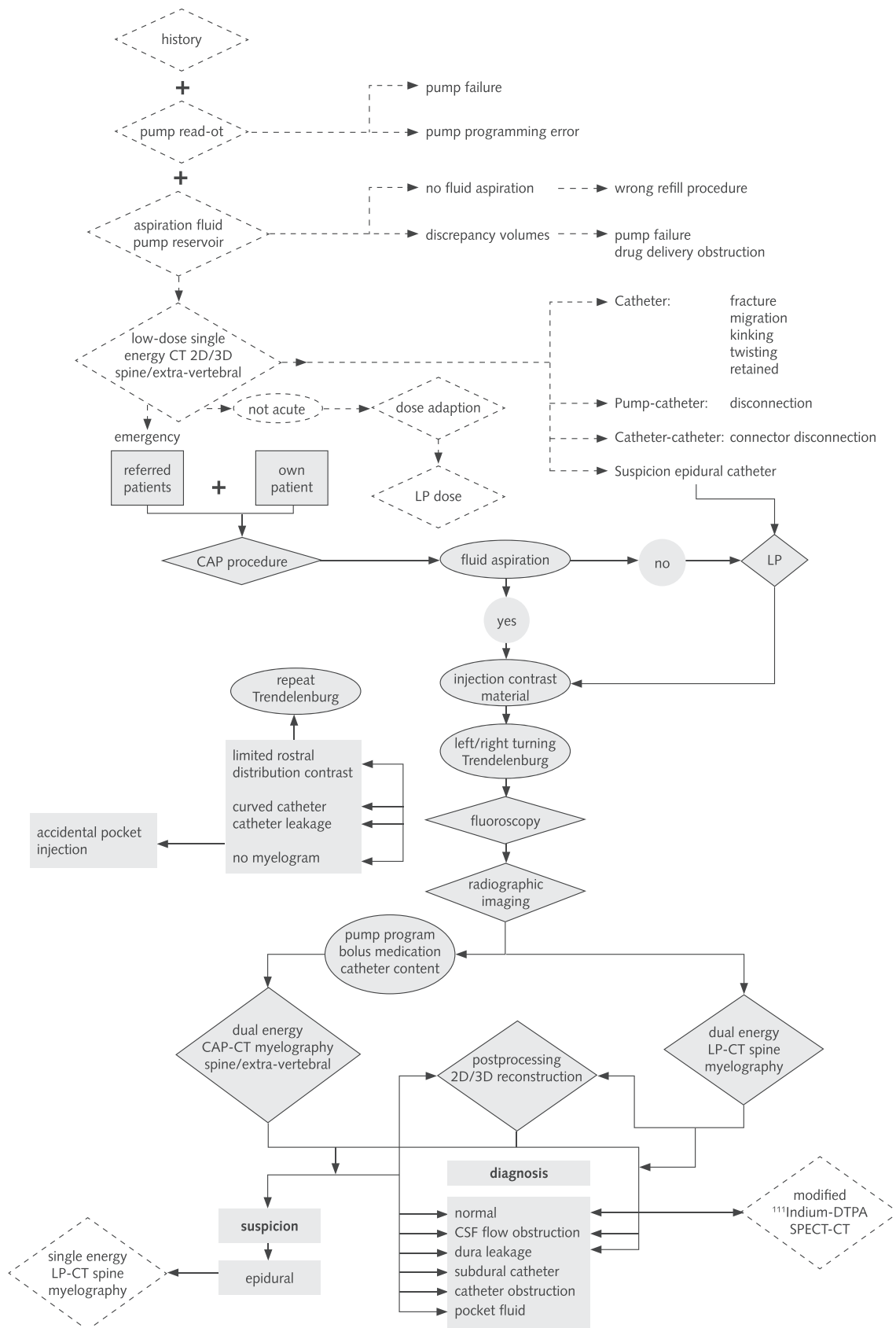


Figure 8. Applied algorithm in intrathecal drug delivery failure.

purposes, we confirmed the importance of CAP-CT myelography in diagnosing the causes of ITDD failure. With CAP handling, there is potentially the risk of intoxication should the highly concentrated medication in the intrathecal catheter not be completely aspirated or of withdrawal when after the procedure the intrathecal catheter is not refilled by a programmed bolus injection of the medication. We found that, when the algorithm is followed, the procedure could be performed safely. Together with the results presented in a recent publication, the data of the study indicate the need for a revision of the algorithm used (Fig. 8). The changes include a replacement of plain radiography by low-dose CT with 2D/3D reconstructions in first-line troubleshooting. Applying this type of CT, the standard dose non-contrast CT, which we performed when fluid could not be aspirated via the CAP provide no additional information and was therefore removed from our algorithm. Instead of the standard dose noncontrast CT, we will apply lumbar puncture myelography, which offers more reliable information about an epidural catheter and also allows for the identification of an obstruction in the spinal canal.

CAP Procedure

The identification of a catheter obstruction, an epidural or subdural catheter position, or a pump-catheter disconnection where fluid could be aspirated, was potentially misleading, as it could lead to the unjustified conclusion that a catheter is functional. The respective explanations could be as follows: a partial catheter obstruction allowed fluid aspiration; at the epidural catheter position, the aspirated fluid was not CSF but the drug solution; the subdural catheter position was associated with a minor amount of intrathecal CSF; and, in a pump-catheter disconnection, the aspirated fluid was present in the pump pocket. When fluid cannot be aspirated via the CAP of the pump, it does not always indicate a catheter obstruction or a disconnection (25), as we confirmed in nearly half of the cases. We cannot offer a convincing explanation; perhaps it is a matter of catheter collapse during aspiration or catheter holes positions close to the dura wall. We initially terminated the CAP procedure when the fluid could not be aspirated. When unsuccessful CAP aspiration is aborted due to an inability to aspirate fluid, no reprogramming of the device needs to be performed.

CAP Myelography

This study confirmed that an appropriate diagnosis or the identification of an abnormality can often not be made with CAP fluoroscopy and myelography only, which limits their value when not routinely followed by CAP-CT myelography. Therefore, the use of CAP-CT myelography alone has been suggested (26). In addition, in our study, the value of CAP-myelography was limited; only two diagnoses, which were subsequently confirmed with spinal/abdominal CAP-CT-myelography, were made. However, fluoroscopy provides a screening overview that makes it possible to identify sufficient intrathecal distribution of contrast material, which is crucial for an optimal diagnostic CT myelography examination. An optimal distribution of contrast material can be achieved through rotation and turning of the patient in different directions, including the Trendelenburg position. An inadequate distribution of contrast material could result in an abnormal examination, as the limited distribution may be misinterpreted as a CSF flow obstruction. Therefore, when fluoroscopy reveals

insufficient contrast material distribution in the intrathecal space, the Trendelenburg maneuver should be performed again.

CAP-CT Myelography

Through the use of CT myelography extended with 2D maximum intensity projection/multiplanar reformation and 3D post-processing reconstructions based on the volume-rendering technique, we achieved substantial improvement in diagnostic accuracy. The demonstrated sensitivity and specificity of the spinal CT myelography examinations indicated the usefulness of the proposed procedure. However, the extra-vertebral parts of the ITDD system should be included in the reconstructed field of view to detect leaks in the catheter pathway and accumulations of contrast material in the pump pocket and their causes. In an identified dura leak, an unexpected finding was caused by retrograde flow of CSF and contrast material along the implanted catheter. This observation means that, in cases of pocket fluid accumulation, a dural leak should be considered. Furthermore, the symptomatology of a dural leak varies from tremendous manifest dropping CSF leak to silent, sometimes chronic, not clinically recognized dural leak with and without complaints of post-dural puncture headache. We could manage the dural leaks with one to three epidural homolog blood patches.

The reduction of beam-hardening artifacts when using dual-energy CT facilitated the identification and cause of fluid in the pump pocket and leaks at the metal catheter-catheter connection. However, beam-hardening reduction should be used carefully when a leak in the pump pocket, which can cause more irregular scattering that resembles beam hardening, is suspected. A leak may be overlooked when a strong beam-hardening reduction algorithm is applied. With the correct beam-hardening reduction, the observed fluid in the pump pocket makes multisession scintigraphy unnecessary.

Accumulation of the contrast material in the subdural space was observed with a faint distribution in the intrathecal space due to a subdural catheter location was observed in only two cases. We therefore could not confirm the reported 18.9% (12). The limited intrathecal contrast material can explain the surprising finding of CSF aspiration in a dural catheter position. The subdural cavity between the meningeal layer of the dura mater and the inner arachnoid mater of the leptomeninges, which are adherent to each other, usually does not exist (27). A potential explanation is unintentional separation during puncture (28,29).

In all of the patients with an unintended epidural catheter, the cause was not a dural perforation at the tip of the catheter but an epidural position starting at the dural insertion. Despite the epidural location, aspiration of 2 mL via the CAP was possible. It seems that, despite low-volume infusion, epidural fluid accumulation occurs when tissue absorption is insufficient, which is likely related to epidural fibrosis as a result of long-term infusion (30–32).

We prefer our modified dual-energy spinal/abdominal CAP-CT-myelography as the initial step in advanced imaging algorithm and reserved scintigraphy for the next. CAP-CT-myelography offers excellent possibilities in terms of identifying flow obstruction, catheter kinking, and leaks, as well as the cause(s) thereof, and a diagnosis often can be made based on a one-day procedure. The latter is a major advantage for severely handicapped patients for whom traveling is a burden. Theoretically, further advantages are that puncturing the CAP provides an opportunity to aspirate CSF for diagnostic microbiological and

pharmacological examinations. CAP-CT myelography generally provides more local information than low-dose energy ^{111}In -DTPA SPECT-CT. In dural and catheter leaks, the more detailed images of CAP-CT myelography are essential in treatment. A few patients refused further imaging procedures; the consequence was that we had to draw our conclusions based on clinical criteria and not on diagnostic imaging.

Additional Imaging Procedures

When we could not assess the cause of ITDD failure with CAP-CT myelography, we proceeded with other imaging modalities. In the study, standard noncontrast CT was helpful for the diagnosis of epidural catheter position when fluid could not be aspirated via the CAP and CAP-CT myelography was therefore not allowed. When using the revised algorithm and low-dose CT, there is no longer any reason to perform this procedure. MRI was used to exclude granuloma formation at the tip of the catheter, and lumbar puncture CT myelography was used to identify CSF fluid obstruction or when in doubt of the epidural catheter position with standard noncontrast CT. In particular, when we needed dynamic information concerning catheter flow or the distribution of intrathecal contrast material, we performed modified ^{111}In -DTPA SPECT-CT scintigraphy.

With this modification, we standardized the flow rate to establish a norm for tracer transit time. As we found, this information is crucial for identifying partial obstruction, as a result of which delayed and/or reduced rostral visibility could be overlooked. Therefore, we disagree with the statement that an examination is normal when the tracer activity progresses to the cerebral cisterns without leakage. As we observed, the clinical relevance of a partial obstruction in CSF flow could be difficult to interpret with CAP-CT-myelography, and the additional dynamic flow information provided by scintigraphy could prove valuable in deciding whether or not to carry out an intervention. We found that, despite a limited leak, tracer activity can reach the intrathecal space. However, the ITDD failure indicates that the amount of

medication in the CSF was probably insufficient for a successful treatment. More publications will probably offer clarity about the observation. After identifying normal rostral distribution with scintigraphy, we accepted the finding of the curved catheter in the intrathecal space as normal in the absence of further complications (33). Although scintigraphy was not performed in all patients, the observed high accuracy of ^{111}In -DTPA SPECT-CT leaves it open to discussion whether the primary choice for ITDD troubleshooting should be CAP-CT myelography or ^{111}In -DTPA SPECT CT scintigraphy (11). We prefer our modified dual-energy CT myelography, as it offers excellent possibilities in terms of identifying flow obstruction, catheter kinking, and leak. Further advantages are that puncturing the CAP provides an opportunity to aspirate CSF for diagnostic microbiological and pharmacological examinations. For therapeutic purposes, the intrathecal catheter content can be aspirated after an overdose or for complex dose concentration changes. Moreover, a bolus dose of the current medication, an additional drug, or contrast material for controlling the ITDD can be injected via the CAP. CAP-CT myelography generally provides more local information than low-dose ^{111}In -DTPA SPECT-CT. In dural and catheter leaks, the more detailed images provided by CAP-CT myelography are essential in treatment. However, ^{111}In -DTPA SPECT-CT is helpful when no fluid can be aspirated via the CAP. In addition, when a normal-shaped limited flow is identified and there is no certainty that the Trendelenburg position has been appropriately performed, scintigraphy can be used to visualize the physiologic fluid distribution. In both methods, however, identifying fluid in the pump pocket can be an issue. In CAP-CT myelography, pump scattering can mask the presence of fluid, although the irregular scattering of fluid differs from that of beam hardening caused by the pump. This problem can be overcome by reducing the scattering via advanced CT techniques such as DECT. We found that, in ^{111}In -DTPA SPECT-CT, the intense tracer activity in the pump is not an obstacle to assessing aberrant fluid in or nearby the implanted pump with the use of image scaling and the progression of fluid accumulation during multiple imaging sessions. Hence, we

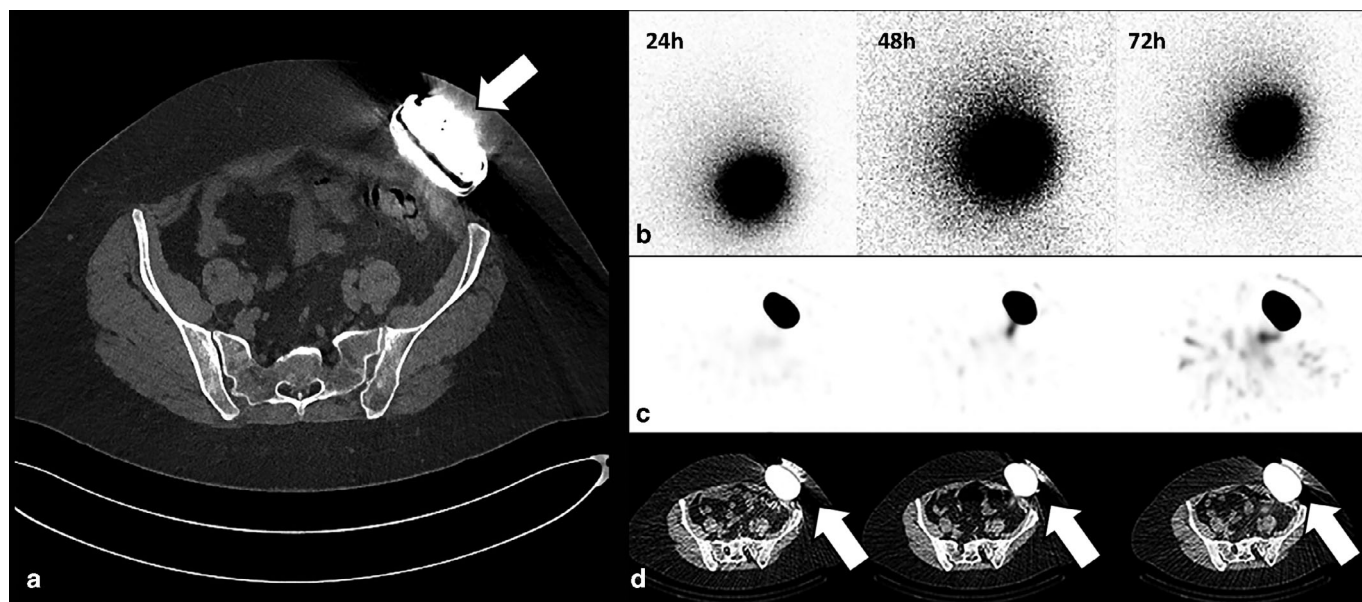


Figure 9. Dual-energy catheter access port CT myelography with metal artifact reduction with irregular scattering (a, white arrow) showing fluid in pump pocket. Additional ^{111}In -DTPA scintigraphy: planar imaging (b) pump failure or leakage, SPECT (c), and CT progressive minor deformation suspect for leakage.

disagree with those who advocate reserving the CAP-CT procedure only for emergencies and using ^{111}In -DTPA in all nonacute situations (11). In our opinion, scintigraphy is a crucial step in the troubleshooting algorithm when a diagnosis cannot be made with CAP-CT myelography or when in doubt and confirmation is required, but it does not outweigh the convenience and accuracy of a CAP-CT myelographic procedure, even when one does not consider the burden placed on the patient, the costs, and the low likelihood of availability in every center. A few patients refused further imaging procedures, with the consequence being that we had to draw our final conclusion based on clinical criteria and not on diagnostic imaging. The finding of a pocket leak while tracer activity was also found in the intrathecal space was intriguing.

CAP-CT Myelography and ^{111}In Indium-DTPA Scintigraphy-SPECT

In our opinion, CAP-CT myelography and ^{111}In Indium-DTPA scintigraphy are not entirely comparable. However, both have their place in ITDD troubleshooting. With the current knowledge of and experience with dual-energy CAP-CT myelography with iMAR, the image (Fig. 9) would be assessed as fluid in the pump pocket (see also Fig. 4). At that time at which the image was created, there was doubt as to whether the image indicated beam hardening or fluid in the pocket. Additional ^{111}In Indium-DTPA scintigraphy-SPECT was performed, which indicated the presence of fluid in the pocket, but this finding was not completely convincing. Surgical interventional demonstrated a sheared catheter localized in the pump pocket. Today with our optimized CT procedure, we would not have carried out additional scintigraphy. The opposite was the situation where we identified an obstruction in the intrathecal contrast material distribution using CAP-CT myelography. Initially, it was concluded that the obstruction was not the reason for ITDD failure. To ascertain normal medication delivery and the absence of bias caused by a forced injection of contrast material, additional scintigraphy was performed. While performing the scintigraphy, we standardized the pump flow such that the catheter tip would be reached at 24 hours. The observed high thoracic gradient on the planar images and the reduced cerebral cisternal tracer activity confirmed stagnation of distribution, and the SPECT-CT imaging showed an almost complete intrathecal stop. While imitating normal intrathecal flow functional drug delivery hindrance could be demonstrated with scintigraphy. We concluded that this observation was likely the cause of ITDD failure.

STUDY LIMITATIONS

The analysis of the observational routinely collected data was intended to evaluate the diagnostic role of CAP-CT myelography in ITDD failure and to improve the procedure by omitting high-dose non-contrast CT, ameliorating imaging with the standard use of dual-energy CT with metal artifact reduction, post-processing the 2D/3D reconstructions, and evaluating its results. A limitation is that the data analysis could not be addressed using existing reporting guidelines such as STrengthening the Reporting of OBServational studies in Epidemiology (STROBE) (34). Nevertheless, routinely collected data are frequently used to improve patient care and health care efficiency. To our knowledge, our study is the most extensive analysis to date; however, the sample size is small. In addition, the retrospective character of this research presents a chronology bias (35); how this might have

influenced our conclusions must be considered. To reduce misclassification bias, all images were reassessed. The most important limitation is the unstructured approach to data collection, which resulted in the absence of a standardized reference test based on a second imaging modality or surgery to determine the actual cause of ITB failure. Instead, we composed the reference based on all available data, including the index test, additional imaging modalities, surgery, and wait-and-see results.

CONCLUSIONS

Despite the bias in the design of this study, the data suggest that CAP myelography followed by CAP-CT myelography are indispensable steps in determining the causes of ITDD treatment failure. The premises of this study are as follows:

- CAP dual-energy CT myelography with image reconstructions of the spinal and extra-vertebral regions in combination with 2D multiplanar reformation/maximum intensity projection and 3D volume-rendering technique reconstructions is an advanced imaging procedure for cases involving ITDD failure.
- Failure to aspirate CSF via the CAP does not indicate catheter failure in all cases.
- Conducting CAP myelography alone is insufficient for the diagnosis of ITDD failure; however, it has value in facilitating needle insertion of the CAP and as a screening method for determining sufficient distribution of the contrast material, which is crucial in a diagnostic CAP-CT myelography.

Authorship Statement

Dr. Delhaas, Dr. Harhangi, Professor van der Lugt and Prof. Huygen designed the study. Dr. Delhaas conducted the study, including patient recruitment and data collection. Dr. Frankema and Professor Huygen were involved in patient recruitment. Dr. Delhaas and Professor van der Lugt were involved in data analysis and prepared the manuscript draft with important intellectual input from Dr. Harhangi, Dr. Frankema, and Professor Huygen. All authors approved the final manuscript. All authors had complete access to the study data.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the supporting information tab for this article.

COMMENT

The authors present impactful information that informs clinicians who manage ITDDS as our specialized community in neuromodulation moves toward more standardization in the management ITDD to reduce variability between clinicians and ultimately improve patient safety and outcomes.

Gail McGlothlen, DNP, RN
Napa, CA, USA